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TUBERCULOSIS OF THE BREAST

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TUBERCULOSIS of the breast is a relatively rare condition when compared with the frequency of tuberculous infection and tuberculous disease in other organs of the human body. Yet it is not so uncommon among the diseases of the breast. In the Mayo clinic from 1904 to 1915, there were 10 cases of mammary tuberculosis reported, or 0.51 per cent of all the mammary conditions that had been admitted to the hospital. Of the 1,500 cases of mammary diseases that entered the St. Bartholomew's Hospital, London, 1.5 per cent were tuberculosis of the breast. H. B. Barker in 1926 stated that although only 15 cases were recorded from the University Hospital, it was interesting to note that the department of pathology showed a total of 62 cases of mammary tuberculosis from all sources, or one case to each 45 of malignancy. Gatewood found it present in 1.04 per cent of all breast cases which were operated upon at the Presbyterian Hospital of Chicago. These figures compare closely with those of Scott who showed one case of tuberculosis to every 50 cases of carcinoma of the breast. Bloodgood found it present in 6 per cent of the benign lesions of the breast. The rarity of tuberculosis of the breast is, therefore, apparent rather than real, and arises from the condition being overlooked.

In reviewing the literature on this subject, I have found more than 439 cases, of which 238 cases were primary and 157 were secondary; 42 were considered doubtful. Almost all of these were proved either by microscopic examination or the finding of the causative factor, namely the tubercle bacillus either in the tissue itself or in the pus derived from the lesion or in some cases by both methods substantiated by positive animal inoculation. There also has been a number of other cases reported at an earlier date which had no pathological proofs and which I shall only mention in passing. Furthermore, this disease is not limited to the female sex. There has been 20 cases of tuberculosis of the breast in the male including the one reported by me.

The differentiation between the primary and the secondary forms is rather a difficult problem. We must consider a case primary if there is a complete absence of a previous history of tuberculosis involving any part of the body (i.e. lungs, glands, bones, etc.). Furthermore, on examination in a particular case there must be absolutely no evidence of the presence of either a latent or active tuberculous focus except in the involved breast. A secondary case is one in which the patient at some time or other has had evidence of a Koch infection or still has an existing tuberculosis in some other organ. As there is no record of a patient coming to necropsy with tuberculosis confined to the breast, absolute proof of a single case of primary tuberculosis arising in the mammary gland is still lacking. Gatewood, in 1916, suggested that those cases,

like tuberculosis of the kidney, might be said to be deuteropathic, in the sense that the lesion is secondary to some unrecognized focus elsewhere, in contradistinction to the exceptional case, which may really be primary or protopathic.

In his famous work on diseases of the breast, Sir Astley Cooper, in 1829, was the first to recognize mammary tuberculosis as a clinical entity. He spoke of this condition as a "scrofulous swelling of the busom." However, Virchow, at a later date denied that the breast is vulnerable to tuberculosis. Nélaton, in 1839, recognized the fact that mammary tuberculosis might occur as the only lesion of its kind and owe its existence not to a contiguous process or to a more distant lesion of like nature, but to sources apart from these. Bérard reported a case in 1842, but gave no new data and no pathological proofs. In 1851, Heyfelder was the first to report a case in the male. Johannet, in 1853, reported a case in a woman who also suffered from tuberculosis of the lung. Velpeau, in 1854, reported 4 cases and distinguished three forms of the disease, namely: disseminated tuberculosis, lymphatic tumors, and lymphatic degeneration. Givaldes, in 1854, and Bauchet, in 1857, discussed the condition but did not add anything new to the problem. Lancereaux, in 1860, described a case and was the first to base his diagnosis not only on clinical findings but on the microscopic appearance of the breast tissue. Bazin mentioned the subject in his *Lexicon sur la Scrofula* in 1861. Cuneo, in 1868, described a case occurring in a male and I believe was not only the first to have isolated the organism from the pus but was also the first to have practiced successfully animal inoculation with positive results. Jamain, in 1870, cited Velpeau and also concluded that this disease must be extremely rare. Other authors, such as Holmes, Voillemier, Robert, and others, discussed this condition but contributed no new details. Horteloup, in 1872, reported another case in the male but gave no pathological proofs. Koster, in 1873, stated that he found macroscopically a distinct tubercle in a case of mammary abscess. Eric Ericson, in 1874, mentions in passing Velpeau's work on breast tuberculosis. Leger, in 1878, reported a case of breast tuberculosis in a woman who died of a generalized Koch infection. He, however, gave no pathological proofs. Billroth and Richet discussed the subject thoroughly in 1880, and Klotz during the same year reported 3 cases, 1 of which was primary. One of his cases he proved with microscopic examination.

The second epic in the study of mammary gland tuberculosis began with the presentation of Dubar's thesis in 1881, when a diagnosis was based not only on a histological examination but also on the finding of the tubercle bacillus in the tissues. He reported 2 new cases and described two forms of the disease, namely the isolated or disseminated nodular type and the confluent type. He regarded the first form as more apt to be primary in the breast. His report established the first definite criterion for the microscopic recognition of tuberculosis of the mammary gland. Following this dissertation, many more authors published and described cases of breast tuberculosis, among which were Duret, in 1882; Crandall, in 1883; Poirier, in 1883; Ohnacker, in 1883; Durante, in 1884; Orthmann, in 1885; Habermass, in 1886; Souplet, in 1886; and Mollier during the same year. Piskacek published 8 cases in 1887, two of which were primary. It now became recognized as a distinct clinical entity so that authors began to look for this condition among the diseases of the breast, and numerous cases were reported as outlined in the tables to follow.

Roux, in 1891, gave a complete review of the cases with 3 additional cases in 2 of which he was successful in isolating the organism. Furthermore, he described the third form of the disease which he called "intraglandular cold abscess." Robinson, in 1892, considered the mode of origin of this disease concluding that it was not primarily an infection of the glands proper but first of the connective tissue and later of the gland epithelium, the evidence being in favor of a lymphatic or hæmatogenous origin rather than a duct infection. In 1893, Remy and Noel published the report of a case of this disease occurring in a woman aged 53 years, the most advanced age recorded to that time. Powers, in 1894, reported 35 collected

cases and showed that the disease was evenly distributed in the third, fourth, and fifth decades of life. He found that 21 of the 22 married women had borne children and 9 had given a history of previous inflammatory changes in that breast. He volunteered the belief that the puerperal state and subsequent lactation were not without predisposing influences upon the cause of the disease. Sabrazes and Binaud, in 1896, gave a most complete pathological and histological résumé of tuberculosis of the breast, together with a review of the literature. Freiberg, in 1898, and Smith, in 1902, reported cases that seemed examples of secondary involvement of the breast by extension from the axillary glands through the lymphatics to the breast tissue.

There is a good deal of controversy in regard to the mode of infection in cases of mammary tuberculosis. The possible paths of infection are: (1) through the ducts, (2) through a surface wound, (3) through the blood stream, (4) through the lymphatics, and (5) through the contiguity of structures.

The possibility of the entrance of the specific organism into the breast through the nipple and the ducts is rather a remote one. The skin rarely harbors the Koch bacillus in a viable state for any length of time. A number of cases have been reported in which infection took place in this manner. Ingier cites a case in which the inflammation was confined to the walls of the excretory ducts and the periacinous tissue, the interacinous tissue being only slightly involved. Ely, in 1890, mentions a case in a woman who had covered her breast with a piece of linen that was contaminated with tuberculous sputum and soon after developed tuberculosis of that breast. He believed that the bacilli had been carried into the openings of the galactiferous ducts through the nipple. Rodman believes that inasmuch as the lesions are more pronounced in the alveoli than in the ducts, and furthermore, as the ducts are not more diseased at their exit at the nipple than in the substance of the gland, it is questionable whether infection through the ducts is common. Gatewood, however, states that this does not necessarily follow, as tuberculosis of the tongue is very rare, and the process when present begins in the muscular septa in spite of the fact that the glands and the mucosa of the tongue are areas which are most frequently exposed to the tubercular organism. The case of the male which I am reporting in this paper is no doubt a distinct example of this mode of infection. His habit of pinching his nipples for the peculiar "twang" which it gave him was instrumental in the infection. The histological examination of the specimens showed distinct evidence of tuberculosis in the excretory ducts.

It is quite plausible that accidental infection may take place through a surface wound of the breast. This lesion might be tuberculous from the very beginning or become secondarily infected with tuberculous sputum. Fricke, in 1907, reports a case in a woman 56 years of age who had no tuberculosis elsewhere in the body but complained of a small lump in her breast. Her husband who had pulmonary tuberculosis massaged the growth with ointments and when the breast was removed, it showed carcinoma and tuberculosis. Fricke believed that the tuberculosis was implanted by her husband and, therefore, must have been secondary to the carcinoma. The infection might have taken place either through the ducts or through the skin. Ravenel has shown that the tubercle bacillus is able to pass through the skin or mucosa without leaving any signs of its invasion.

The majority of investigators have considered that mammary tuberculosis is of hæmatogenous origin. That, of course, would be the most simple explanation of a primary infection in the breast. It is rather difficult to understand why the organism after having gained its entrance in the blood stream should localize itself in the breast tissue, an environment least conducive to its growth and multiplication. Furthermore, it would preclude that there must have been a primary focus elsewhere in the body from which source the organism had entered the circulation. This in itself would make all breast tuberculosis secondary to other foci. Nagaskima, in 1925, reported 34 cases of disseminated tuberculosis of the miliary type which had come to autopsy. He made sections of all suspicious breasts but did not find tuberculosis in any of the cases.

He concluded that a hæmatogenous infection of the breast with tuberculosis must be extremely rare, in that, the breast appeared to be the only organ that was spared in his series of cases. He further made a bacteriological examination of these breasts and failed to show the organism. He also injected the mammary extracts into guinea pigs and could not induce tuberculosis in any of the animals.

Halstead and LeCount state that in about 75 per cent of the cases reported there was a tuberculous adenopathy affecting the axillary glands on the same side as the breast lesion. Many authors were of the opinion that the majority of cases of mammary tuberculosis were the result of a retrograde lymphatic involvement from the axilla or from some intrathoracic focus. This belief was based upon the observation that in a number of instances the involvement of the axillary nodes seemed definitely to precede the mammary involvement, and this opinion is strengthened through the recognition of the intimate relationship of the mammary gland to the axillary and mediastinal lymph nodes. Illustrative of this point is the interesting case of Duvergey, quoted by Deaver. This patient, while washing the linens of tuberculous patients, abraded a finger of her left hand. The wound suppurated for 2 weeks and then healed completely. Eight months later she noticed a swelling in the left axilla which was incised, and from which pus was evacuated. The wound did not heal and 3 months later a painful lump appeared in the left breast. This was drained from time to time, other sinuses developing in the breast during the treatment. The lungs eventually became involved and the tubercle bacillus was isolated in the discharge from the sinuses. Here the evidence strongly points to a retrograde lymph-vascular infection. Scheidegger describes a case of carcinoma and tuberculosis in the breast of a woman 37 years of age. The axillary glands were tuberculous but not carcinomatous. He believed that the carcinoma of the breast was primary but the tuberculosis was secondary, the primary focus being in the axillary glands. Fischer, in a similar case in a woman aged 69 years, reported the finding of tuberculosis in the axillary glands and a lump in the breast. Amputation showed a carcinoma of the breast with secondary tuberculosis originating from the axillary glands. In 8 cases of the 37 reported by Berchtold, the disease was primary in the axillary glands and secondarily involved the mammary gland. This was regarded by Verneuil as the usual mode of infection of the breast. However, it may be said that the primary focus in the breast in many cases escapes notice until after the axillary glands are considerably involved. Again, the disease in the axillary glands, when secondary, usually advances with greater rapidity than that of the mammary gland, so that while the axillary glands may be broken down and suppurating, the nodule in the breast may remain stationary for a considerable length of time. Fuller maintains that the demonstration of the origin in many cases of tuberculosis of the breast is, therefore, the purest guess work and will be an impossible task unless the disease is plainly a contiguous process from some nearby organ or tissue. Reerink also believes that most cases of tuberculosis are secondary to axillary tuberculosis. In Johannet's case which came to autopsy, there was a subpleural tuberculosis which had extended to the axillary glands and then to the breast. Duret, in 1882, was the first to recognize this mode of infection and described a case in a woman 32 years of age who since the age of 12 had enlarged glands of the axilla which after marriage gradually enlarged to the size of an apple and then extended via an indurated cord-like infiltration involving the breast on the same side. Raw cited the case of a girl aged 19 years who was admitted to the hospital with very extensive tuberculosis of the right glands of the neck. She had been brought up in Canada and had used very large quantities of unsterilized milk in the previous 12 years. The infection had spread by direct lymphatic extension to the axillary glands which had suppurated, and thence to the breast, which was in a condition of generalized tuberculous mastitis with 5 sinuses discharging a large amount of pus daily. He concluded that mammary tuberculosis is never primary but is the result of a lymphatic extension from the glands of the neck or axilla excepting in rare cases of generalized miliary tuberculosis. He furthermore

believed that it was caused by the bovine bacillus. Gatewood stated that in the light of recent observation upon the occurrence of localized infections caused by blood borne organisms, it would seem that almost all cases of tuberculosis of the breast are but secondary manifestations of a tuberculosis elsewhere. In reviewing the cases of breast tuberculosis, disregarding whether they were considered primary or secondary by the authors, I found that among the 439 cases reported, including my own 6, 236 showed distinct axillary involvement. These figures are not exact, as some authors failed to mention whether the glands were involved or not; therefore, in view of the relative frequency of tuberculous adenitis when compared with tuberculosis of the breast, it is most probable that the majority of cases are due to a retrograde lymphatic involvement, either from the axilla or from a primary focus in the thorax by the way of Grossman's path and Rotter's lymph nodes. Furthermore, I do not believe that it is possible to rule out completely a tuberculous focus in the lung even if the patient has been subjected to a most thorough physical examination including roentgen examination of the chest. It is a well known fact that the majority of people are infected with the Koch bacillus but not diseased. These organisms no doubt may remain in the body for a long time in a latent state and suddenly become aroused into activity due to a diminished local resistance in some particular portion of the body. The lymphatic glandular system about the hilus of the lung is known to have harbored these organisms over a long period of time causing little or no symptoms. It is quite plausible then, that the infecting agent may pass from this locality, through a retrograde process via the lymphatic system, and reach the breast. The history and subsequent changes found in mammary tuberculosis certainly points toward this manner of infection.

Infection via the contiguity of tissues is a mode of infection readily understandable and requires no further elucidation. A number of cases in the literature have been reported in which the process spread from a diseased rib or a tuberculous caries of the sternum.

A number of authors, among whom are Raw and Barker, have come to the conclusion that most cases of mammary tuberculosis are caused by the bovine tubercle bacillus. Barker, in 1926 stated, "All cases in which the type of the bacillus has been determined were proved to be of the bovine type, but the number of cases from which the bacilli have been cultured is much too small to warrant conclusions." If we bear in mind that the bovine bacillus has a predilection for the lymphoid tissue of the human body, it is not surprising that tuberculous mastitis is caused by this particular type of organism, especially if we consider that the path of infection is through the lymph channels from the glands of the axilla. However, the so called secondary cases in which the primary lesion is in the lung are more apt to be due to the human type of the tubercle bacillus.

Among the etiological factors in breast tuberculosis, it appears that trauma plays a very minor part. We must bear in mind that due to the anatomical position of the breasts, they are naturally exposed to injury at frequent intervals, yet among the 439 cases reviewed only 32 gave a history of some form of injury. This is only 7 per cent. If injury is to be considered a factor in predisposing an area to tuberculosis by reducing the tissue vitality, then the breast is just as liable to this infection as any other organ, particularly when there exists a tuberculous focus elsewhere in the body.

Heredity also plays no great part as a predisposing factor. Only 13 per cent of the cases reported gave a history of tuberculosis in the family. There is not a doubt that it plays a greater part in the so called secondary forms where the patient has or had pulmonary tuberculosis. Here heredity plays the same part as it does in phthisis.

Breast tuberculosis is more frequent during the active sexual period of life. It is, therefore, found in the second, third, and fourth decades. It is extremely rare before the tenth year and fairly uncommon after the age of 50 years. After making a thorough survey of this particular angle, I was able to accumulate the following data:

Of the 439 cases reported in the literature, the youngest patient was that of Demme who

reported finding mammary tuberculosis in a male infant aged 6 months. This was proved with microscopic examination and the finding of Koch bacillus in the tissue and further borne out by positive animal inoculation. No cases were reported between the ages of 1 and 10. One hundred twenty-seven cases occurred between the ages of 20 and 30. An almost equal number, i.e., 131, occurred between the ages 30 and 40. From there on the frequency diminished. Only 83 cases of mammary tuberculosis were recorded between the ages of 40 and 50; 32 were found between the ages of 50 and 60; 9 between the ages of 60 and 70; and 2 between the ages of 70 and 80. The oldest was the case reported by Shield, a woman 73 years old. In conclusion, therefore, it may be said that the greatest age incident of mammary tuberculosis is between 20 and 40 years. This is very important to bear in mind and should be an aid in differentiating mammary tuberculosis from mammary carcinoma.

There is a slight tendency for the right breast to be more frequently affected than the left. Two hundred and four cases showed right breast involvement whereas only 175 showed left breast involvement. Nineteen cases had bilateral involvement.

There is no doubt that the marriage state with the consequent puerperium and lactation plays more or less an important part as a predisposing factor in breast tuberculosis. In this series I noted that 285 had been married of whom 180 had borne children. Only 81 cases of breast tuberculosis occurred in single women. However, we must consider that the greatest majority of women between the ages of 20 and 40 are married and that is just the age that mammary tuberculosis occurs with greatest frequency.

There is no one single pathognomonic symptom or sign of mammary tuberculosis but taken all together they present a fairly distinct picture which in most cases should lead to a correct diagnosis. I certainly disagree with Fuller who in 1909 stated: "Taken as a whole, nothing is so misleading about disease in general as symptoms, and this applies abundantly to tuberculosis of the breast. The symptoms in no two cases are the same. No two patients describe symptoms alike and no two observers construe them alike." One of the most important symptoms that the patient complains of and the very first he or she notices, is a lump in the breast. This was the first thing that 290 patients noticed of the 439 cases here reviewed. This sign had occurred long before they had observed any discomfort or pain. The other signs and symptoms usually vary with the type of the infection and the course which it takes. Barker, in 1926, classified this disease clinically as follows: (1) breast tuberculosis with rapid evolution, (2) breast tuberclosis with slow evolution, and (3) sclerosing type or pseudoneoplasm.

The lump usually occurs in the upper and outer quadrant of the breast. It may be present for a long time before the patient consults a physician. As long as it is stationary it is usually neglected, only when it begins to increase in size and begins to give some pain is it brought to the attention of the patient sufficiently for them to consult their doctor. In this series 132 had noticed this lump for 6 months or less. Ninety-seven had noticed the presence of a lump for more than 6 months. It had been present in one case as long as 8 years, and in another almost 14 years. This mass in the breast is usually insidious in its onset and free from pain until it distends the surrounding tissues with its growth, or the overlying skin becomes involved. A characteristic feature of the disseminated nodular type is the extreme chronicity of its process and its painless and insidious development. The breast is usually not enlarged, and on palpation masses are felt resembling small adenomata. The confluent type occurs as a further step in the pathological process and this variety shows a more acute course. This form is frequently seen in the lactating breast. The skin over the involved area becomes tense and reddened and the patient begins to complain of severe pain due to the distention of the underlying tissues. It usually breaks through and a fistula forms, discharging a thick cheesy pus. This may persist over a long period of time until the infection spreads and other fistulæ form, either connecting with the first or originating from other broken down areas in the breast. The sclerosing type of tuberculous mastitis, seen

most frequently in elderly women, is similar to the fibroid type of tuberculosis found elsewhere in the body. Here the breast is apt to be distorted and the nipple retracted and the lesion, if palpable, is of firm consistency. This form has been very aptly called the tuberculous pseudoneoplasm of Chauvin and can very easily be mistaken for a scirrhous carcinoma. The disease may take this form either because of low virulence of the infecting organism or because of the greater resistence of the host. It spreads rather rapidly to the axillary glands, and although the process in the breast appears to be more or less stationary, the axillary glands rapidly go on to caseation. The intraglandular cold abscess of Roux is usually a terminal product of the confluent form of tuberculosis which has not broken through because of its deep seated location. In several cases the earlier symptoms and the course of the mammary involvement varied from the usual form. In Orthmann's case, it began apparently subcutaneously and resembled an ordinary furuncle. In Poirier's case it began as a number of vesiculated pimples with indurated bases. In Kramer's, an ulcer first appeared near the nipple, later nodules formed within the breast and were connected to the ulcer by bands of indurated tissue.

Pain as an early sign in breast tuberculosis is fairly uncommon. It occurred in only 6 per cent of the cases reviewed. It is present in almost all the cases when the mass has grown sufficiently or has broken down. Retraction of the nipple is fairly rare and is found only in those cases in which the tuberculous process occurs in or around the areola and also in the so called scirrhous form of breast tuberculosis in which the process is of long duration and of low virulence. Here it depends upon the excessive formation of connective tissue and its retraction with resultant deformity of the nipple. This symptom is the one that frequently leads to the mistaken diagnosis of carcinoma of the breast. A few patients complain of a distinct tenderness in the nipple occurring when it comes in contact with their clothing and causes them extreme annoyance.

Swelling of the glands of the axilla involving the same side is one of the most frequent signs of mammary tuberculosis. This is noticed in many cases even before the patient's attention has been attracted to her breast. It may precede the breast involvement by many months but is usually not sufficiently annoying to bring the patient to her physician. The axillary lymph nodes may or may not be the seat of tuberculosis. A palpable gland does not necessarily mean tuberculosis nor does a nonpalpable node mean the absence of tuberculosis. Of the 439 cases reviewed, 236 showed glandular involvement, many of which were positive for tuberculosis on histological examination. This certainly points to the possibility that the infection arises there and involves the breast secondarily. The glands frequently go on to earlier suppuration while the mass in the breast remains more or less stationary.

Contrary to the statement of many authors that this disease affects only the spare, weakly, anæmic individuals of the so called scrofulous diathesis, I found that the greatest majority of cases occurred in women of robust character who had always maintained an excellent state of health. However, this holds good only for the so called primary type. The secondary form of mammary tuberculosis does occur in those patients who have a predisposition to tuberculosis and in whose family there is a history of tuberculosis. Two hundred and twenty-eight were in good health, 66 were in fair health, and 69 were in poor health, the latter occurring only in those cases who had other active foci of tuberculosis.

The course of the disease is usually a progressive one and the rapidity of its progress is greatly dependent upon the type and pathological form that the disease takes. No case is known to have undergone spontaneous regression after it once has started. In this manner it differs from phthisis. It is, therefore, purely a form of surgical tuberculosis and always requires intervention. The nodular type may remain stationary for years, but once it begins to advance, there is a steady increase in the size of the tumor. The confluent type shows a more acute course with early breaking down and abscess formation. Here it may be a question of weeks, especially if it occurs during the lactation period. In this form it frequently spreads toward the axilla with which it is joined by masses or bands of indurated tissue.

This occurred in the cases of Mandry, Piskacek, Hebb, and others. Without intervention, the process continues by extension, involving new areas before the older ones have healed and death more or less slowly advances when the disease is left to itself, particularly through the involvement of the thoracic viscera. Vandel, in 1927, stated that the average duration of the disease varied from 10.1 months in the primary cases to 11.2 to 12 months in the secondary cases. On the whole, mammary tuberculosis pursues a more rapid course than mammary carcinoma.

There are few, or almost no, complications in mammary tuberculosis except that the disease, if left to itself, continually progresses invading the neighboring organs.

Tuberculosis of the breast is sometimes associated with other diseases of the breast. Among the cases reviewed about 5 showed the presence of adenomata, a number showed fibro-adenomata, and over 15 showed carcinoma. The latter is of great importance as it may be overlooked and a conservative operation be performed with the belief that we are dealing only with a Koch infection. The interpretation of their relationship is of great interest as several possibilities exist.

1. The two conditions may occur independently of one another, either simultaneously or consecutively.

2. The tuberculosis may be engrafted upon the malignant process as a result of the breaking down of the tissue with a resultant increased susceptibility of the area to tuberculosis.

3. The carcinoma may be the result of the chronic irritation of the tuberculous inflammatory process.

In the case of Smith and Mason the carcinoma seemed to be the lesion of longer duration, as it was a typical scirrhous type for the most part and the tuberculous lesion showed no calcification. It thus suggests the second possibility cited, that of a tuberculous process superimposed on a degenerated malignant disease. Bundschuh, in 1913, discussing the association of these 2 conditions, is of similar opinion as Smith and Mason. Other authors, among whom are Klose, Fricke, Scheidegger, Kallenberger, Moak, Schifone, etc., reported similar findings. The doctrine set forth by Rokitansky that carcinoma and tuberculosis are never found in the same patient, and as later modified by Dietrich and Martius, that both of these processes never appeared in the same organ, has long been exploded. Friedlander, Wolfe, and Schwalbe have described the occurrence of carcinoma in lung caverns in cases of chronic pulmonary tuberculosis. Lubarsch found multiple carcinomata of the ileum, showing tuberculous infiltration, and metastatic carcinoma in areas of fresh tuberculous infiltrations of the lung.

The correct diagnosis of tuberculosis of the breast is of utmost importance, and its early recognition may save the patient from a radical operation. It cannot be stated in better words than those used by Manley: "To one advanced in years the pathetic deformity following the clearing away of an atrophic nonfunctionating breast is a matter of little consequence, but to the young unmarried woman, it is on the contrary, most serious, for she is no longer a complete woman stripped of Cupid's most inestimable adornments." Furthermore, its accurate detection at once relieves the patient of the dreadful apprehension of cancer and leads to a safe and radical measure of treatment devoid of danger to life. The clinical findings are not always sufficient to aid the physician to make a correct diagnosis. A lump in the breast of long duration not associated with pain or retraction of the nipple but associated with glandular enlargement is very suggestive. If to this is added the presence of a fistula discharging a gritty caseous material, one can fairly safely make the diagnosis of breast tuberculosis. Fistulæ are present in about 50 per cent of the cases and are quite characteristic of this condition. The demonstration of the bacillus in the discharge or in the tissue is accomplished with great difficulty. Mammary tuberculosis belongs to the group known as the bacillary poor processes. Piskacek was able to find only a few bacilli in 400 preparations, and of the 79 cases collected by Deaver, the bacilli were found in the stained sections only 7 times, and in the preparations of pus only 4 times. In my review, I found that the organism had been isolated in about 100 cases which is about 25 per cent of the cases

reported. This is no doubt due to the better methods now employed and the more improved staining procedures.

Breast tuberculosis must be differentiated from a number of other conditions that may give a similar picture. Among these are chronic mastitis, cystic mastitis, the so called galactocele, fibroma, adenoma, sarcoma, and carcinoma. The first five conditions mentioned usually show no glandular involvement. Sarcoma grows with much greater rapidity and is extremely rare. Pain is usually a very prominent symptom, and the cutaneous veins of the breast are usually greatly dilated and engorged. In adenofibroma, the growth of the tumor is very slow as in the nodular variety of tuberculosis but differs from it in that the former is freely movable in the breast. Carcinoma, of course, is rather difficult to differentiate from breast tuberculosis. Even in cases in which there is a distinct fluctuation, one cannot rule out cancer as this tumor may undergo central softening. However, it usually occurs at a later age, it frequently causes deformity of the nipple with some retraction, and the patient complains of pain. The safest procedure in the differential diagnosis is the removal of a small portion for histological examination.

The prognosis in mammary tuberculosis is excellent if the diseased area is completely eradicated. Braendle, in 1906, reviewed a number of cases and showed that there were no recurrences except in a single case in which the operative intervention was much too conservative.

The following methods of treatment have been employed in the cases reviewed: (1) curetting of the sinus, (2) cauterization of the sinuses, (3) injection of the sinuses and cavities, (4) incision and aspiration of abscesses, (5) removal of the tumor alone, (6) removal of the axillary glands alone, (7) removal of the tumor and portion of the breast, (8) removal of the breast completely, (9) removal of the breast and axillary gland.

I personally believe that the treatment depends upon the individual case. With early involvement and early diagnosis, the more conservative operation may be all that is necessary to save the patient.

The pathology of breast tuberculosis is similar to the pathology of tuberculosis elsewhere in the body except for some variations due to the histological structure of this organ. The pathological changes may pursue certain forms and these are best classified as follows: (1) acute miliary tuberculous mastitis, (2) nodular tuberculous mastitis, (3) disseminated nodular tuberculous mastitis, (4) confluent tuberculous mastitis, (5) intraglandular cold abscess, (6) sclerosing tuberculous mastitis, (7) tuberculous mastitis obliterans.

In the acute miliary tuberculous mastitis, the breast is affected in a similar manner to other organs of the body. This form is comparatively rare as has been shown by Nagaskima. The breast appears to be the organ most frequently spared in miliary tuberculosis.

The nodular tuberculous mastitis is the most frequent form of breast tuberculosis. The organism having gained entrance into the breast excites a local reaction with the formation of a discreet tubercle. This tubercle is usually situated in the connective tissue and rarely in the wall of the duct or periductal tissue. The lymphocytic infiltration usually extends and involves the acini causing a destruction of the glandular elements. It usually enlarges very gradually until it forms a mass the size of a hen's egg or even larger. There is still some controversy whether the initial lesion occurs in the stroma or in the acini. On section of the individual nodule, we find a bluish grey mass with a central wax colored caseous material which does not convey the gritty sensation as is commonly found in carcinoma. On microscopic examination, there is revealed a mass of caseous substance surrounded by lymphocytic infiltration, epithelioid cells, and a number of typical Langhans' giant cells with peripherally located nuclei. The caseated material may be either firm or have undergone liquefaction. When this takes place, it usually seeks an outlet with the formation of a sinus. As a rule this nodule remains unattached to the skin until the sinus tract forms. If it happens to occur in the areola it may cause retraction of the nipple. This lesion may remain dormant for a long time and then suddenly begin to grow and involve adjacent areas.

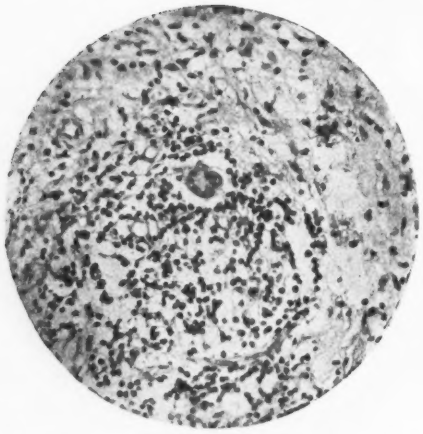

Fig. 1. Young discreet tubercle before caseation has taken place, showing the typical Langhans' giant cell. Case 1. Chart No. 9292.

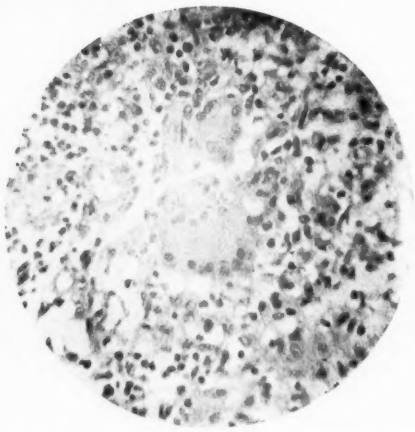

Fig. 2. Area of confluent tuberculosis showing the specific change. Case 1.

The disseminated nodular tuberculous mastitis is just a further step of the simple nodular type with the formation of daughter tubercles from the original mother tubercle. After they break down they usually form multiple sinuses draining individual abscess cavities. It is more acute in its progress and frequently attacks lactating breasts. There is a good deal of destruction of the breast tissue. With coalescing of the individual tubercles, we come to the fourth variety of confluent tuberculous mastitis.

The breast in the confluent type is usually enlarged. On section one finds irregular cavities communicating with each other and filled with a grumous necrotic cellular débris. In the walls of the cavities varying sizes of tubercles are seen, also arising from the walls are fringes and villosities of necrotic material. The membrane lining these cavities is greyish in color. From lactiferous ducts adjacent to these areas there may be expressed grumous material similar to that found in the cavities. On microscopic examination of such areas one notes a center of amorphous hyaline material surrounded by a number of giant and epithelioid cells between which there is a proliferation of new connective tissue and thin walled blood vessels. Fistulæ usually connect these cavities with the exterior.

The intraglandular cold abscess is nothing more than a deep seated confluent tuberculous mastitis well walled off from the exterior in a more or less quiescent stage. The process is slower in its progress but gradually works its way toward the surface to form a fistulous tract. The necrotic material may undergo encapsulation and hyalinization.

The sclerosing type of tuberculous mastitis is a very slow progressive lesion and is easily mistaken for scirrhous carcinoma. The breast is usually not enlarged, but there are a number of very hardened nodules which tend to be attached to the underlying structures and even to the skin. It usually causes retraction of the nipple because of the increased formation of connective tissue. The acini are destroyed and replaced by fibrous tissue. There is usually a diffuse lymphocytic cellular infiltration accompanied by epithelioid and giant cells but very little caseation. The individual tubercles tend to heal and undergo hyalinization but new daughter tubercles form. The breast may shrink to half of its normal size. The axillary glands become involved early and may undergo caseation. This type is usually due to the low virulence of the organism and has been compared to fibroid phthisis because it is also found most frequently in elderly people. Sinuses are of rare occurrence, and the diffe en-

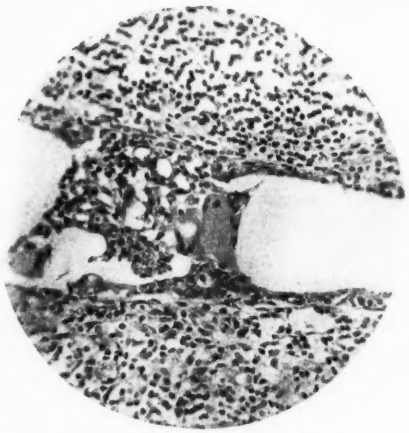

Fig. 3. Tuberculosis affecting one of the galactiferous ducts showing the typical Langhans' giant cell. Case 1.

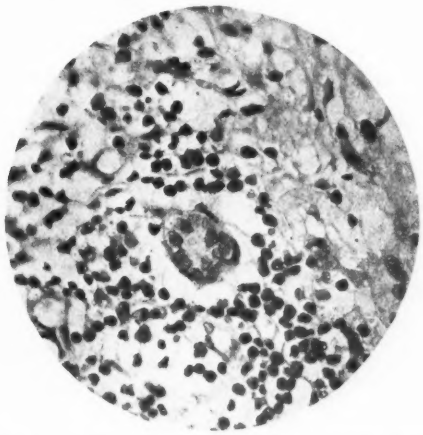

Fig. 4. High power discreet tubercle showing typical giant cell. Case 1.

tiation between this form and carcinoma is extremely difficult.

The tuberculous mastitis obliterans is a variety of mammary tuberculosis in which the lesions seem chiefly to surround the milk ducts, destroying the epithelial linings, filling the lumens with products of tuberculous transformations, and finally obliterating them. One must be careful not to mistake certain forms of mastitis for tuberculosis. In these cases due to the obliteration of the ducts, material containing lipoids become stagnated and excite the formation of foreign body giant cells or the so called pseudoxanthoma cells.

SUMMARY

In summarizing this subject certain outstanding features must be kept in mind some of which are as follows:

1. The rarity of tuberculosis of the breast is apparent rather than real, and arises from the condition being overlooked.

2. The classification of mammary tuberculosis into primary and secondary forms is fundamentally unscientific in that there is no absolute criterion and proof whether a case is primary or not, even if there is no clinical evidence of tuberculosis elsewhere in the body.

3. The most plausible mode of infection is via the lymphatics through a retrograde process, the original site being either in the glands of the neck or the glandular tissue about the hilus of the lung.

4. It occurs most frequently during the active sexual period of life.

5. Its symptoms are varied, the most frequent being a lump in the upper, outer quadrant associated with axillary involvement but no pain until it enlarges sufficiently, breaks down, and forms a fistulous tract.

6. The prognosis is good with early recognition of the disease and its eradication by surgical intervention.

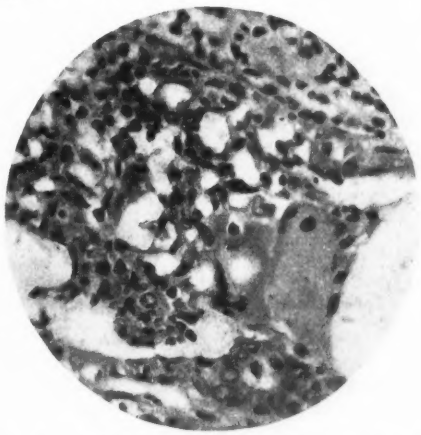

Fig. 5. High power of area showing tuberculous involvement of one of the ducts. Case 1.

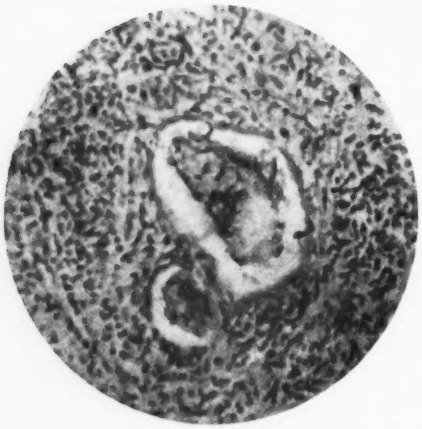

Fig. 6. Tubercle with beginning calcification and foreign body giant cell. Case 4. Chart No. 9324.

7. The pathology is similar to pathology of tuberculosis elsewhere in the body except for some minute differences due to the histological structure of the breast.

The following cases, of which there are 5 female and 1 male, were treated at the Sydenham Hospital.

CASE REPORTS

CASE 1. Mrs. A. L., No. 9292, married, aged 43 years, was admitted to the hospital June 9, 1929, with a diagnosis of carcinoma of left breast. She complained of a painful lump, which she first noticed 8 weeks ago, associated with a marked sensitivity of the left nipple to touch. This lump had progressively enlarged until her entrance to the hospital. Her past personal history was unimportant except for a hysterectomy and appendectomy 10 years previous. Physical examination showed a well developed female adult. There was absolutely no evidence of any pathology except in the involved breast. There was a mass the size of a small orange in the lower outer quadrant of the breast. The skin over it was erythematous but not adherent. It was quite tender to touch. The glands of the left axilla were distinctly palpable. A radical mastectomy was performed with division of the pectoralis major and minor and with dissection of the axillary glands. The wound was closed in the usual manner. The mass of neoplastic tissue was about 3 inches in diameter located external to the nipple. It was firm in consistency but some areas showed evidence of broken down necrotic material. Sections made from numerous blocks of the breast showed varied pictures. Some areas showed evidence of chronic cystic mastitis and other areas showed diffuse necrosis with lymphocytic infiltration and still other sections showed a perfectly typical picture of tubercles with central areas of caseation surrounded by epithelioid and giant cells.

CASE 2. Mrs. H. H., No. 8011, married, aged 33 years, was admitted to the hospital on February 20, 1928, suffering from a small, tender mass in the left breast, which had broken down and was discharging. She first noticed this in June, 1927, when the mass was the size of a bean and was located in the upper outer quadrant of the left breast. It was attached to the skin but caused little discomfort and was, therefore, ignored. A few months previous to her entrance to the hospital, the mass appeared larger and began to discharge. The patient had received X-ray treatments and following the treatments the mass broke down and another mass appeared which simultaneously broke down and discharged. Wet dressings were applied and finally curettage was resorted to with no amelioration of the symptoms. An operation was performed and microscopic examination revealed the following: The breast tissue showed marked fibrotic changes with the bands of connective tissue surrounding the individual lobules and penetrating the same. This resulted in pressure atrophy of the individual glandular elements. Other areas showed diffuse lymphocytic and small round cell infiltration among which numerous plasma cells were to be found. Other areas, however, showed distinct tubercle formations with central areas of necrosis surrounded by small round cells, epithelioid cells and on the outer borders by the typical giant cells of Langhans' type with their nuclei arranged along the periphery of the cell bodies.

CASE 3. Mrs. E. S., No. 15031, married, aged 50 years, was admitted to the hospital on September 10, 1930, complaining of a lump in her left breast. Examination revealed no evidence of any pathological changes anywhere else in the body. Operation was performed and a tumor was shelled out. The gross appearance was that of benign cystic mass. Microscopic examination revealed a typical picture of tuberculous mastitis.

CASE 4. Mrs. R. K., No. 9384, aged 30 years, married, was admitted June 16, 1929, with a diagnosis of tuberculosis of the left breast. Patient complained of pain in the left breast for the last 3 weeks and also noticed that a hard lump had formed. This pain gradually diminished but the lump grew in size. The patient had been weaning her baby for the past 10 months and still had milk in both breasts. This patient had three children. Complete examination of the patient was negative except for the local condition. This showed a hard lump about the size of a walnut in the outer and upper quadrant of the left breast. There was some involvement of the axillary glands. The patient was operated upon and excision of the tumor was performed. Pathological examination revealed very little normal breast tissue left. The whole breast was composed of many tubercles with necrotic areas and a diffuse cellular infiltration among which were epithelioid, plasma, and giant cells.

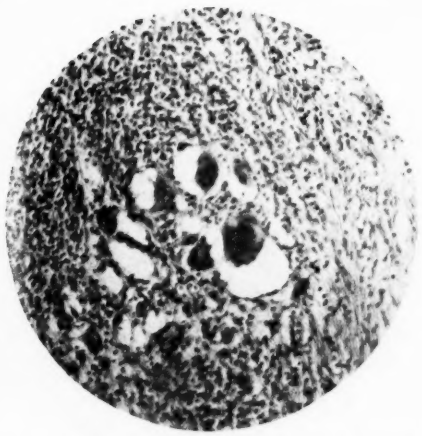

Fig. 7. Low power of non-tuberculous area with pseudo-xanthoma cells. Case 6. Chart No. 1968.

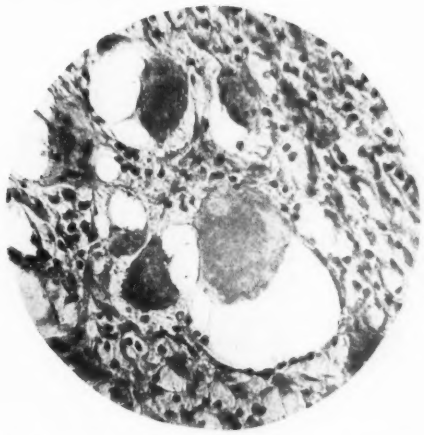

Fig. 8. High power of non-tuberculous area with pseudo-xanthoma cells often mistaken for tuberculosis. Case 6. Chart No. 1968.

CASE 5. Mrs. C. L., No. 4717, aged 51 years, married, was admitted to the hospital May 17, 1928, and discharged June 4, 1928. She entered the hospital with a diagnosis of tuberculosis of the right breast. Her chief complaint consisted of pain in the left shoulder and a small, hard, nodular lump in the right breast. The history dates back to 4 months ago, when she suffered from a rather severe attack of the grippe following which she developed a rather severe pain poorly localized in the left shoulder. She had been treated by diathermy and local applications with no relief. During an examination 7 weeks ago, a small, painless mass was found in the upper outer quadrant of the right breast. She has been suffering from a mild diabetes for a number of years.

The physical examination including X-ray of the chest was completely negative except for the local condition of the right breast. The pain in the shoulder was attributed to a neuritis following an acute respiratory infection. The mass in the breast was the size of a walnut not attached to the overlying skin and only slightly sensitive. The breast was incised and the cystic mass was enucleated. Microscopic examination showed nodular tuberculous mastitis.

CASE 6. Mr. E. D. E., male, No. 1968, aged 30 years, married, was admitted to the hospital, August 23, 1927, and discharged August 25, 1927. Admission diagnosis was adenoma of the mammary gland. His chief complaint was the presence of a tumor in the right breast for 2 months and a discharging nipple for 2 years. Since the patient could remember he had been accustomed to pinch both his nipples for a peculiar "twang" which they gave him. The nipple gradually enlarged, and 2 years ago began to discharge a milky white and sometimes bloody fluid on pressure of the breast. Quite accidently he noticed a small lump underneath this nipple 2 months ago. It had gradually increased in size, but there had been no redness or pain. A thick, whitish fluid could be expressed from the nipple. There were no other symptoms. His general health was good. Physical examination disclosed a well nourished young man not acutely ill. Complete examination was entirely negative except for the local condition of the right breast and hypertrophy of the nipple of the left breast. He also had a right inguinal hernia. Both nipples were very much hypertrophied. Underneath the right areola there was a hard, non-tender mass, movable over the deeper structures and partially attached to the overlying skin and areola. It was about 2.5 centimeters in diameter, and on pressure a small amount of thick, whitish material could be expressed. The tip of the nipple was eczematous. The axillary glands were not palpable.

The pre-operative diagnosis was chronic mastitis.

The operation consisted of a elliptical incision around the areola down to the muscle, with excision of the tumor mass. It was non-adherent and was easily dissected away intact. The skin was closed with interrupted silk.

The pathological report at that time was that of chronic mastitis with abscess formation. On reviewing the slides on breast tumors, I found that it was a typical case of tuberculosis of the nodular type and with distinct tubercle formations and central caseation.

In conclusion, I wish to thank Dr. A. Eisenberg, director, who so kindly furnished me with the available material at the Sydenham Hospital.

Bibliography and table with cases from the literature will be published in full in the reprint.

CYSTIC DEVELOPMENT IN THE SEMILUNAR CARTILAGES

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THE development of cysts in the semilunar cartilages of the knee joint was described in 1904 (2), but only during the last decade has it been appreciated as a not very uncommon clinical condition. A considerable number of cases have been reported, either singly or in groups, and now are within the experience of most surgeons.

The clinical characteristics are well defined but there has been no unanimity of opinion concerning the nature or origin of the cysts. Since some of the features of their development appear to have been overlooked and because some of the observations have been too casual or have been misinterpreted, this note is submitted.

Cysts of the semilunar cartilages occur much more commonly in males than in females, are more commonly associated with the external than the internal meniscus, and have been found slightly more frequently in the left than in the right knee. The condition may be bilateral (personal observation).

The age of the patient is not related to the onset of the condition, since it may be found in young children or old men. Trauma, of a more or less definite character, is found in the history of the majority of the cases. After the onset of the condition, the cysts rapidly progress until they reach a certain size, when they become stationary. Osteo-arthritis in the same joint may be an associated lesion, but apparently is independent.

Surgical treatment, consisting of removal of the cysts and the cartilage, results in cure.

After removal, the cysts are found in the tissue on the outer aspect of the cartilages. Of course, on account of their position, actual cysts cannot be found clinically in the cartilages, but sometimes spaces may be found in them which communicate with the cysts proper. The cysts which are multiple vary from minute spaces just visible to the naked eye to those measuring half an inch or more in diameter.

Microscopically, the cyst walls are composed of fibrous connective tissue or fibrocartilage and are lined with a tissue containing elongate cells, which have been described

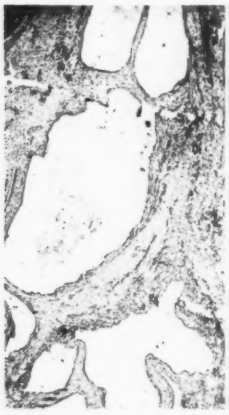

Fig. 1.

Fig. 2.

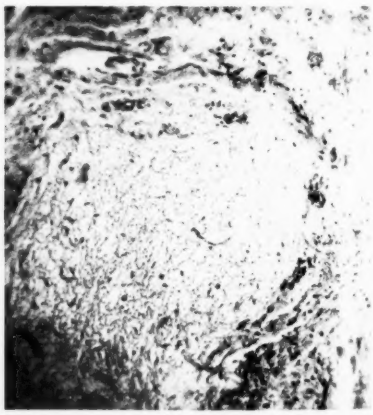

Fig. 3.

Fig. 1. Low power photomicrograph of a section taken from an example of typical cyst of the semilunar cartilage (external). ×12.

Fig. 2. Photomicrograph of a portion of the wall of one cyst. The lining is fibrous connective tissue, the cells being embedded in this, and not lying on the surface. ×30.

Fig. 3. An area of "mucoid degeneration" occurring in the tissue at the outer border of a semilunar cartilage. A few cells may be seen in this tissue. (See Figs. 4 and 5.) ×30.

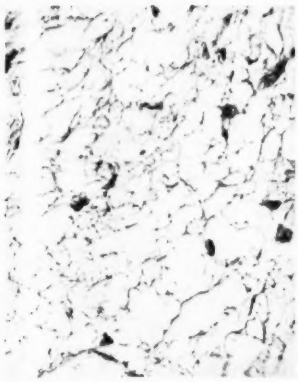

Fig. 4.

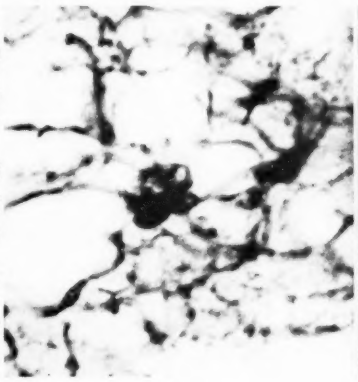

Fig. 5.

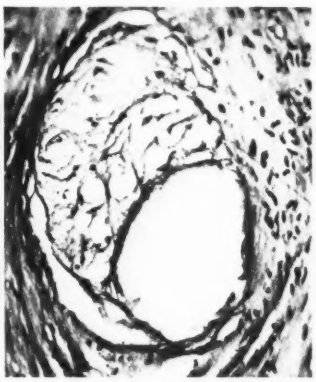

Fig. 6.

Fig. 4. Higher power view of the tissue shown in Figure 3. The tissue is of the mucoid type and contains large cells. ×155.

Fig. 5. High power photomicrograph of the tissue and one of the cells shown in Figure 4. The cell shows no sign of degeneration. The cell outline is well marked and the nucleus is well formed. There are droplets of fluid material in the protoplasm. ×525.

Fig. 6. Photomicrograph of another portion showing a mucoid area and commencing cyst formation. ×155.

variously as connective tissue and as endothelium.

HYPOTHESES OF ORIGIN

The principle hypotheses put forward are:

1. Congenital origin (Ollerenshaw).
2. Lymphatic origin (Kleinberg).
3. Degeneration of cartilage (Allison and O'Connor).
4. Cysts are analogous with ganglia (Ebner, Schmidt).

These hypotheses fall naturally into 2 groups. Hypotheses 1 and 2 rest on the assumption that the cells lining the cysts are endothelial in nature; 3 and 4 depend upon the connective tissue nature of the lining of the cysts.

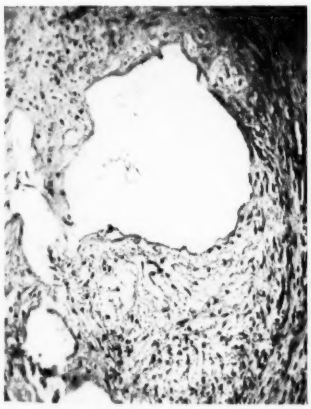

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 7. A mucoid area in the fibrocartilaginous tissue showing early cyst formation. The cyst is lined with tissue which contains spindle cells, most of which lie in the tissue but a few of which are on the surface. ×95.

Fig. 8. Photomicrograph of a section which indicates one method of enlargement of the cysts, by coalescence of the adjacent spaces. The broken septum is quite apparent. ×56.

Fig. 9. Portion of a loculated cyst, showing the typical appearance of the wall. In a few places the cells line the surface but in most places they occur only in the deeper layers. ×70.

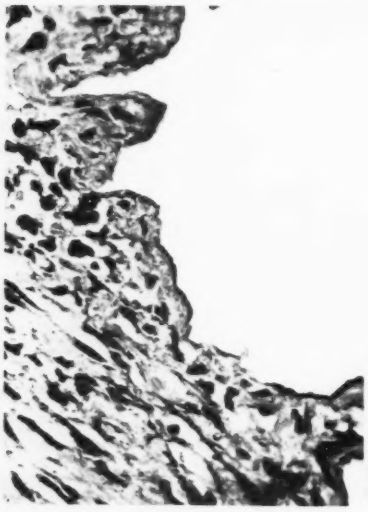

Fig. 10.

Fig. 11.

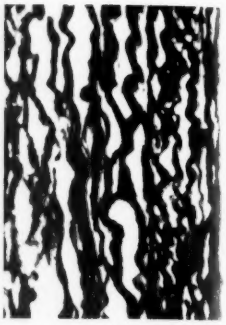

Fig. 12.

Fig. 10. Photomicrograph of the appearance which is typical of the wall of these cysts. The dark line on the surface is a refractive phenomenon and not due to the presence of nuclear material. ×450.

Fig. 11. Photomicrograph of a section of a cyst in which the tissue is collagenous and many of the nuclei rest on the surface. Such areas are continuous with those in which there are no nuclei on the surface for considerable distances. ×540.

Fig. 12. Photomicrograph of a section of a cyst wall after impregnation with silver. The connective tissue (which is impregnated) is seen to go right up to the surface. (Compare Fig. 13). ×900.

Fig. 13.

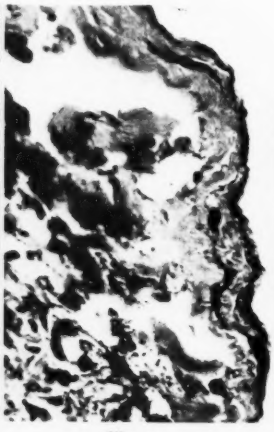

Fig. 14.

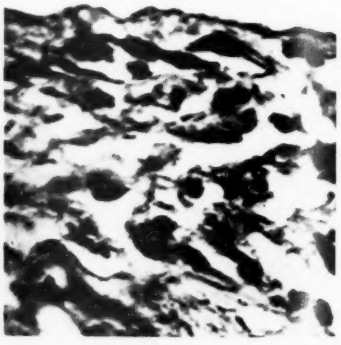

Fig. 15.

Fig. 13. Photomicrograph of a section of a blood vessel taken from the same specimen as that used for Figure 12. The silver does not stain the endothelial lining. The spaces also indicate the position of cells. ×875.

Fig. 14. Portion of another cyst wall. The cells which lie on the surface are seen to do so only in part, a portion of their nuclei running into the deeper tissue. ×525.

Fig. 15. A typical appearance of portion of the wall of a cyst. The structure is identical with that of synovial membrane. ×1050.

The determination of the actual type of cell is not difficult, since staining by the silver methods allows of a differentiation between connective tissue and endothelium. Investigation by means of ordinary stains is not conclusive but, even judging by the morpho-

logical appearances, it is apparent that the lining is not endothelium. This will be discussed further.

NATURE OF JOINT TISSUES

Since pathology is abnormal anatomy and physiology, it is axiomatic that disease of any portion of the body can be understood only when the normal development, structure, and function are elucidated.

The cells of the synovial membrane are modified connective tissue cells which, on account of their position, have become altered structurally and physiologically.

Synovial membrane is different embryologically from either the endothelium of the cœlom or from the endothelium of the lymphatics. Joints arise as a split in an area of "condensation" of the mesenchyme between developing bones.

Structurally, synovial membrane is characteristic. The cells, unlike those of endothelium, do not usually lie on the surface but are embedded in collagenous tissue and, though some may lie close to the surface, the majority are situated deeply. In some parts, cells lie on the surface in part or a cell process may reach the surface. In other parts, some of the cells may lie on the surface completely and resemble endothelium, but careful examination will distinguish these, since the cells are not in apposition, but show fibrous tissue between the cell bodies on the exposed surface.

The cells are spindle, long or short, or spheroidal in shape. They have deeply staining nuclei, and the cells possess large, well defined, protoplasmic processes. Other features have been discussed in other papers.

Physiologically, the synovial surface differs from endothelium. A mucoid material (synovial fluid) is secreted, which differs from any material derived from endothelium. The mode of secretion is still undetermined, but droplets may be found in the protoplasm of the synovial membrane cells.

Another, though much less significant, point is that complete removal of the synovial membrane of a joint is followed by complete restoration of the synovial membrane after a few weeks. This suggests that the membrane is merely modified connective tissue.

Since the tissue lining joint cavities is a specialized connective tissue and not endothelium, it might be expected that lesions occurring in synovial membrane would show special modifications of this connective tissue rather than the development of cells occurring, as far as this region is concerned, only in lymphatic and blood vessels.

MICROSCOPIC APPEARANCES OF THE CYSTS

The sections of the specimens were examined following staining by hæmatoxylin and eosin, hæmatoxylin and Van Gieson, and several modifications of the silver impregnation methods. Various appearances were encountered which were interpreted as being different stages in the same process. These will be described in order of development.

Areas of varying though usually small size, in which the tissue was homogeneous with but few fibrous strands, were found throughout the sections (Fig. 3). Very few cells were present in this material (Fig. 4). These were large, spheroidal, with well formed nuclei, and contained fluid droplets (Fig. 5). The material stained like mucoid tissue; the surrounding tissue gradually merged into the mucoid areas.

Cystic spaces were present in some portions of the tissue described (Figs. 6 and 7). These spaces are lined, in part by endothelium-like cells and in other parts by connective tissue only (Figs. 9, 10, and 11).

All gradations could be observed between these small cysts and the larger cysts which have only connective tissue in the wall.

The larger cysts are lined by connective tissue and not by endothelium. This is apparent not only from the morphology in hæmatoxylin and eosin sections but also from the sections impregnated by silver (Figs. 12 and 13). In these the surface material is seen in most cases to be the actual fibrous tissue and the cells are embedded in the fibrous tissue stroma (Fig. 15). A few lie on the surface but these do not constitute an endothelium (Fig. 14).

Cysts of varying size were found in close connection with each other and in many cases, adjacent cysts had become continuous with each other as shown by the presence of septa (Fig. 8).

In the walls of some of the cysts fibrocartilage was present, but the majority showed only fibrous tissue.

DISCUSSION

In the original description and discussion of the condition of cystic development in the semilunar cartilages, Ebner and Schmidt both considered that this was comparable with the ganglia. The evidence is all in support of this opinion but since other hypotheses have been advanced, emphasis of some of the features of these cysts is necessary.

The first problem is the nature of the lining of the cysts. The opinion that the cells are endothelial in character is due to a lack of understanding of the morphology of synovial membrane, inadequate examinations, and the omission of the use of special staining methods. It is a relic of the older views concerning the nature of synovial linings. This is shown by a reference to the current expressions of opinion.

Zadek and Jaffe refer to the "synovial nature of the lining endothelium"—a manifest contradiction in terms. Though some portions of the cysts show cells on the surface, many show cells only embedded in the deeper layers, and these have not been mentioned or explained by some writers. Those who support the hypothesis of the endothelial nature of the lining have not brought forward the necessary evidence by use of special methods. An examination of the photomicrographs of the sections of these authors, indicates that the lining is connective tissue, not endothleium (Ollerenshaw, 6). Since the lining is connective tissue, we may discard the hypothesis that the cysts are of lymphatic nature or origin.

Ollerenshaw has put forward certain statements in support of the view that the cysts are of congenital nature. None of these is proof against critical examination and, in fact, the multiplicity of the cysts suggests an acquired rather than a congenital origin, particularly since all gradations may be found between mucoid tissue without cyst formation and well defined cysts.

The history of trauma in so many cases also supports the view that the cysts are an acquired condition.

The remaining hypotheses (1) that of degeneration in cartilage and (2) that the cysts are comparable with ganglia, are similar. In the first place synovial membrane and the cartilage of joints are similar and closely related tissues. They merge into each other and arise from the same original tissue in the embryo—their morphology being governed by the particular part they play in the joint economy. It is to be expected thus that similar changes would occur in both synovial membrane and fibrocartilage.

The reasons for concluding that the changes are degenerative in nature are (a) that thickened blood vessels are found in the cystic area and (b) that the earlier changes found are "mucoid degeneration" in the connective tissue. On the other hand, vessels of the thickness of those seen in sections of these cysts are found usually in the majority of the affections of synovial membrane, so that they are probably not primary. The areas of "mucoid degeneration" are probably not degenerative, since the cells present in these areas are well formed, in fact, larger than the other cells of the part, and have a well formed nucleus. The protoplasm contains many well marked droplets.

Since similar droplets are present in the cells of synovial membrane and are probably secretory in nature, it is probable that the mucoid areas are the result of secretion of certain of the cells. Examination of examples of ganglion have led me to the conclusion that the process here is also a secretion of the cells, rather than degenerative. In this way the cystic change in the semilunar cartilages is strictly comparable with the change associated with the formation of ganglia. It should be stated here that a differentiation is made between degeneration and an exaggeration of normal secretion, since both the morphological characteristics of the cells and the restoration to their original state indicate that the condition conforms rather to the concept of an exaggeration of a normal process than to a true degeneration.

In résumé, the changes present are as follows: (1) certain cells enlarge and secrete mucoid material into the connective tissue between them; (2) some of this material becomes more fluid and cysts form; (3) these gradually

enlarge and the cells in the neighborhood revert to their original spindle form, some lying on the surface but the majority being embedded in the tissue. Briefly, the tissue, under some stimulus, forms a "joint cavity" which is comparable with a bursa or ganglion.

SUMMARY

1. The development of cysts in semilunar cartilages is described.

2. The lining of the walls is the same as the lining of the synovial membrane, a modified connective tissue and not endothelium.

3. The cysts are comparable with ganglia.

4. The various hypotheses of their origin are discussed.

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THE EFFECTS OF TOTAL GASTRECTOMY

Experimental Achylia Gastrica in Dogs with the Occurrence of a Spontaneous Anæmia and Anæmia of Pregnancy

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IN this paper we desire to report our observations extending over a period of 7 years on the effects of total gastrectomy in the dog.

We have made observations on 14 gastrectomized dogs which have survived 6 months or longer, and on the same number that have succumbed to distemper, enteritis, etc., within 1 to 6 months following the operation. Of the 14 dogs surviving longer than 6 months, we have 7 in the laboratory now with the following postoperative survival periods: Dog 3 (Ajax), 6 years, 2 months; Dog 10, 5 years, 3 months; Dog 11, 2 years; Dog 13, 1 year, 9 months; Dog 16, 1 year, 11 months; Dog 26, 6 months; Dog 27, 6 months. Another dog is on hand which has survived 3 months.

This work was started by one of us (Ivy) in collaboration with Drs. Lim and McCarthy (37, 38) primarily for the purpose of studying gastric secretion. For this work dogs with a "pouch of the entire stomach" and a duodenoœsophageal end-to-end anastomosis were desired; and since we have been primarily interested in the question of the mechanism of gastric secretion, most of our dogs have had pouches of the entire stomach (37, 38). However, in 3 of our animals now living (Dogs 10, 11, 13), the stomach was entirely removed from the body, which is an easier operation than to make a pouch of the entire stomach. Either procedure obviously deprives the animal of the digestive functions of the stomach and produces a sudden absolute achylia gastrica, since in either case the food swallowed passes directly from the œsophagus into the duodenum.

The technique of the operation will be described only briefly. The operation is performed in one stage. We have tried a two stage operation, but adhesions caused too much trouble. The pylorus is separated from

the duodenum, the duodenum is closed, the clamp remaining in place on the pylorus. The duodenum is closed because experience has taught us that it is better to suture the end of the œsophagus to the side of the duodenum than to perform an end-to-end anastomosis. The œsophagus is pulled down by traction on the stomach, and a "tunnel" is prepared with the index fingers posterior to the cardiac orifice, to receive one blade of the clamp. The diaphragm is pushed upward (sometimes it is necessary to cut the reflected diaphragmatic peritoneum at this point) and a special clamp serving to close the œsophagus and to elevate it forward is placed on the œsophagus about ½ to ¾ inch above the gastro-œsophageal venous ring. A second clamp is placed on the stomach just below the venous ring. The œsophagus is sectioned about ¼ to ⅜ inch above the venous ring. It is not difficult at this point to observe if the section has been made through the œsophagus or the stomach. At this time the cardia of the stomach is closed if a pouch of the entire stomach is to be made. This is not done if the stomach is to be removed. The duodenum is then brought up to the end of the œsophagus and the œsophagus is anastomosed end-to-side to the duodenum about 1 or 2 inches below the opening of the common bile duct.

Care must be exercised in making the anastomosis so that the duodenum is not kinked, so that it is free and movable, and is not pressed on by the lesser omentum. If the fibrous portion of the diaphragm is injured too much, or if stitches must be taken to prevent pneumothorax, the animal is likely to die of pleurisy or mediastinitis, the stitches generally pulling out. Postoperative pneumonia frequently occurs. Peritonitis occurs infrequently, if the œsophagus can be exposed sufficiently to get a clamp on it, which cannot always be done in the dog, and if the dogs have been fed meat and milk for several days and then fasted 24 hours to insure a "clean" stomach. This is done on the hypothesis, which has been borne out by our experience with other operative procedures on the stomach, that high gastric acidity attenuates virulent organisms (1, 2). This suggests that achylic patients should have their stomachs lavaged with 0.3 per cent hydrochloric acid prior to operation, unless gastric hæmorrhage is known to be present. The day after the operation 400 or 500 cubic centimeters of Ringer's solution are given subcutaneously, on the second day small quantities (10 to 25 cubic centimeters) of warm water by mouth at intervals, and on the third day small quantities of milk at intervals. After this preliminary period, cooked ground meat and bread are gradually added. Our mortality has varied from one period to another. In the first period in which an end-to-end anastomosis was done, 10 dogs were operated upon; the mortality was 40 per cent from all causes, taking one month as the survival time. When we changed to the end-to-side anastomosis (Morgan and Ivy), we operated upon 7 dogs with 2 deaths, 1 death from peritonitis, the other from cachexia. Of these 5 dogs surviving the immediate effects of the operation, only 1 is now alive at 2 years, the others dying of the following causes: 2 of intestinal obstruction due to adhesions, 1 of enteritis, and the other was accidentally killed with tetraiodophenolphthalein. Mr. Morgan then operated upon 5 dogs and 2 are now alive longer than 2 months. Of all dogs operated by our group, 46 per cent have survived 1 month, and 23 per cent 6 months.

Diet. The dogs are fed daily a mixture of ground meat (1 pound) which has been brought to the boiling point, whole milk (300 to 400 cubic centimeters), and baker's bread (½ pound), a diet which we know maintains normal dogs in cages for a period of as long as 6 years in a good state of health. The gastrectomized dogs must be fed about twice the maintenance diet required by a normal dog, because of the considerable amount of undigested residue passed in the fæces. In 3 dogs which we have observed, raw ground meat (½ pound forced fed) passed through the intestinal tract in from 2 to 4 hours, practically without being changed in color. When the meat is brought to a boil, these irritating properties are lost for the most part.

Eating habits. After gastrectomy the eating habits of the dog are immediately changed. Instead of bolting the food, it is eaten slowly, and the daily ration is consumed in from 4 to 12

hours. Even milk is ingested slowly. This change has occurred in every dog in our series. As time passes, however, they eat somewhat more quickly, but our 6 year dog still takes 10 or 12 hours and our 5 year dog 4 to 6 hours to ingest the daily ration. We believe that the slow eating is due to uncomfortable sensations coming from the duodenum produced by overdistention.

Compensatory dilation of the duodenum and œsophagus. Obviously one might expect some compensatory dilatation of the œsophagus and duodenum, especially since Fauley, Strauss, and Ivy have found recently in dogs that if one-half to three-quarters of the stomach is removed, compensatory hypertrophy results in about 6 months in most dogs to the extent that the stomach returns to normal or greater than normal capacity. X-ray evidence in our gastrectomized dogs shows that only a slight dilatation of both duodenum and œsophagus results.

Ulcers. Ulcers of the duodenum have not occurred in any of our dogs, which shows that the undigested food we feed and as ingested does not cause ulcers and that food of the type and consistency ingested in our dogs *per se* is not a likely cause of postoperative jejunal ulcers in man. Recent work on dogs by Fauley, Strauss, and Ivy shows that postoperative jejunal ulcers following subtotal gastrectomy do not occur until the stomach has undergone hypertrophy and free acidity has returned. Neither have ulcers occurred in the pouch of the entire stomach as has been reported by Moutier.

Vomiting. Gastrectomized animals with both gastric vagi cut, but with the thoracocœliac branch of the vagus intact, vomit when the duodenum is irritated. However, vomiting is very difficult and prolonged in these animals. Food particles from the intestine rarely appear in the vomitus. Much bile is present and much air is swallowed, and the vomiting and swallowing movements churn the duodenal secretions and saliva into a heavy dense froth. On one occasion during an attack of vomiting, the intestine was markedly distended with swallowed air so that the abdomen presented the appearance of paralytic ileus. It was possible by exerting pressure on the abdominal wall to expel large quantities of air by mouth. An abdominal binder was applied and gaseous distention was prevented.

Enteritis. Enteritis has been a frequent cause of death in our dogs even among those that survived a period of 6 months. It occurs chiefly during the warm months. For example, 4 dogs were operated upon in November and December. Normal weight and health were maintained until the latter part of June when a period of hot weather occurred. Then diarrhœa developed and all 4 died within 2 weeks, of enteritis. Two other gastrectomized dogs that had been operated upon several years before and other dogs in the kennel were unaffected. Our explanation of the occurrence of enteritis in these animals is that the attenuating and bactericidal action of gastric juice on ingested organisms was absent and that the hot weather permitted the food in the pans to become heavily infected. This explanation is supported by the work of Arnold and Brody on the effect of gastric secretion on the flora of the intestine in that they showed that a preponderance of acid or acidbuffered substances in the upper gastro-intestinal tract caused an auto-disinfection of the exogenous flora, and that hot weather which decreases gastric secretion caused a decrease in this auto-disinfecting phenomenon. Bartle and Harkins have demonstrated that gastric juice has a germicidal value in *in vitro* studies.

Teeth. All our dogs have manifested a marked tendency toward tartar formation and 4 of the 7 dogs on hand now show early evidences of pyorrhœa in spite of cod liver oil administration. The 6 year old gastrectomized dog whose actual age is approximately 7½ years, about 4 years after the operation began losing his teeth, only his molars and one canine being intact at the present time. On removal of the tartar, deposition reappears within 2 weeks. The cause and prevention of the tartar deposition is being investigated in collaboration with Dr. Skillen of the Dental School, the only warranted preliminary statement being that brushing the teeth daily with a fruit containing citric acid prevents deposition of the tartar. It is interesting in this connection that Hobday states that pyorrhœa is very common in house-fed dogs whose diet is

free of bones. No other disturbances of bony structure have been observed. Hurst (32) and others (30, 54) report that pyorrhœa and dental caries are very frequently associated with pernicious anæmia and achylia.

Stomatitis, glossitis, and nervous disturbances. We have examined our dogs for the occurrence of stomatitis, glossitis, and nervous changes, since these conditions are clinically associated with achylia, without finding evidence of such disturbances.

Blood chlorides. In the dogs in which the stomach is retained as a pouch of the entire stomach, from 200 to 400 cubic centimeters of gastric juice is lost daily. This loss of gastric juice obviously might decrease the blood chlorides. An examination of the blood chlorides in these dogs reveals that there occurs a preliminary drop after the operation which returns to normal in about 2 weeks. The preliminary drop is due to the postoperative hypersecretion that occurs in these animals which is also known to occur following the production of a Heidenhain and Pavlov pouch, and to the reduced postoperative intake of chlorides in the food. From 7 to 10 days after the operation the animal is on a full diet in which the chloride intake balances the chloride output, which accounts for the maintenance of a normal blood chloride level.

ANÆMIA

The most interesting and significant finding in these dogs is the occasional development of anæmia. The anæmia has occurred spontaneously in 3 of the 14 dogs and only during pregnancy in 3 others, i.e., 6 of the 14 dogs have developed an anæmia. Of the 6 that developed anæmia, 5 had pouches of the entire stomach and 1 had the stomach removed from the body. The 3 dogs that developed the spontaneous anæmia were males. The anæmia appeared from 6 to 8 months after the operation. We shall record our observations on anæmia under two topics, namely, the spontaneous anæmia and the anæmia of pregnancy.

Spontaneous anæmia. A spontaneous anæmia appeared early in our work on dogs with a pouch of the entire stomach which was begun in January, 1924, in collaboration with Drs. Lim and McCarthy.

The first dog (Dog 1) to develop an anæmia was operated upon in February, 1924. Eight months later it developed an anorexia, loss of weight, and on a study of the blood, manifested an anæmia. The red cell count was 5.6 million, the leucocytes 18,000, and the hæmoglobin 60 per cent. Two weeks later the dog died; the blood findings several days prior to death were: red cells 3,250,000; leucocytes 12,000; hæmoglobin 40 per cent. Autopsy revealed no worms and no cause of death other than anæmia and cachexia.

A second dog (Dog 2) was operated upon August 19, 1924. This animal returned to good health which was maintained until February, 1925. On February 25, the red cells were 6.0 million; leucocytes 11,630; hæmoglobin 45 per cent. On March 5, the red cells were 3.3 million and the hæmoglobin 30 per cent. In this animal therapy was instituted which consisted of iron and cod liver oil by mouth, ultra violet light, and raw and boiled liver by forced feeding. The animal died March 14, very anæmic and cachetic. Autopsy revealed no worms nor additional cause of death.

The third dog (Dog 3, Ajax) was observed very closely for the purpose of detecting the onset of anæmia and starting therapeutic measures early. He was operated upon November 25, 1924 (weight 17.0 kilograms). Four months later the development of anæmia was detected; the red cells were 6.5 million and the hæmoglobin 72 per cent. One month later, the red cells were 5.2 million, whites 22,000 (normal), and the hæmoglobin 52 per cent. Iron carbonate, 15 grains daily by mouth had no effect. After 2 weeks cod liver oil was given by mouth and ferric citrate (ampoule, 1½ grains) subcutaneously every other day. The animal improved in appetite and weight and 2 weeks later the red cells were 7.2 million and the hæmoglobin 60 per cent. The therapy was stopped and milk buffered with hydrochloric acid was given without preventing the return of the anæmia during a period of 8 weeks. Liver (1 pound) was then added to the diet. Since it was found that raw liver caused diarrhœa in the second dog the liver was brought to a boil. The dog ate the liver, but it tended to cause diarrhœa, and by July 20, the dog's weight had fallen to 15.7 kilograms; the red cell count was 4.8 million and the hæmoglobin 50 per cent. The dog was then placed on cod liver oil by mouth and iron subcutaneously. His weight had returned to normal by September 1. The red cell count and hæmoglobin were practically normal. On September 24, with the animal in perfect condition and the body weight 19 kilograms, the iron was discontinued, but the cod liver oil was continued. One month later, the red cell count was 4.3 million, and the hæmoglobin 58 per cent. Four weeks later, November 30, the hæmoglobin had fallen to 50 per cent. Iron citrate was then given and the blood returned to normal in 1 month. This dog has been rendered anæmic on five different occasions, and each time it was found that both cod liver oil *per os* and iron subcutaneously were necessary to

control the anæmia. Ferric citrate 1½ grains once a week was sufficient to hold the hæmoglobin at a normal level. In November, 1929, the dog was taken off the cod liver oil and iron with the result that anæmia appeared. Then liver extract[1], one ampoule (4 grams), was given daily for 1 week. The anæmia disappeared and oddly enough has not recurred for over 1 year, even though the dog has received no cod liver oil and iron. We can offer no explanation for this fact. (It should be pointed out that blood examinations were made much more frequently than shown in these protocols.)

In Dog 3, which we have observed now for over 6 years, the color index during the early periods of anæmia was less than one. As the anæmia developed, the hæmoglobin fell first. However, after the first 2 years this was not the case, the anæmia appearing and persisting with a color index of 1.0 or slightly above 1. The leucocyte count was uniformly low (15,000, when not anæmic 22,000). During the anæmia the blood smears were approximately as follows: definite anisocytosis; no poikilocytosis; no normoblasts; polymorphonuclears, 60 to 70 per cent; small lymphocytes, 5 to 8 perc ent; large lymphocytes, 8 to 11 per cent; eosinophilic polymorphonuclears, 3 to 11 per cent; monocytes, 3 to 10 per cent; meta-myelocytes, 2 to 5 per cent; an occasional myelocyte. Blood smears were shown to Professor Maximow who verified our interpretation that the smears showed definite evidence of mild bone marrow stimulation.

Although we have observed our dogs closely, we have been unable to detect any cause of the spontaneous anæmia such as infection, worms, and diarrhœa. We know that diarrhœa is a contributing and an aggravating cause, but we have observed anæmia in Dog 3 in the absence of diarrhœa. We believe that the anæmia is secondary in type and the opinion is supported by the fact that the anæmia is controlled by cod liver oil and iron. Blood volumes were not followed, but we shall do so in our future work.

The removal of the stomach in the presence of pre-existing anæmia does not prevent but does retard the return of the blood to normal. Dog 11 of our series was kept anæmic for 1 year by the Whipple method of bleeding and feeding a low hæmoglobin building diet. The stomach then was removed and in 3 months the blood was normal on our regular diet. These dogs generally return to normal in 1 month.

Anæmia of pregnancy. In our gastrectomized colony of 8 dogs, we have 4 females. Three of them have become pregnant; Dog 11, three times; Dog 26, once; and Dog 27, once. An anæmia has been caused by the pregnancy each time.

Dog 11 was operated upon February 20, 1929. The stomach and spleen were removed from the body. A spontaneous anæmia did not occur in 3 months. (Red cells 6.6 million, hæmoglobin 98 per cent.) The dog copulated and conceived. At 6 weeks she aborted with red cells 3.2 million; hæmoglobin 56 per cent. She slowly recovered without treatment and 6 months later her red cells were 6.1 million and hæmoglobin 104 per cent. She copulated and conceived again March 26, 1930. Anæmia was detected in 4 weeks. She aborted dead fetuses at 7 weeks with red cells 4.4 million and hæmoglobin 56 per cent, and color index 0.7. In 2 months (without treatment) the red cells had returned to normal but the hæmoglobin had not. At 3 months the red cells and hæmoglobin were normal. On August 25, 1930, she copulated and conceived a third time. Five weeks later the red cells were 4.4 million and hæmoglobin 68 per cent. Liver extract[2] 4 grams daily was then given which was continued for 10 days. The red cells rose to 5.2 million, the hæmoglobin fell to 52 per cent. Cod liver oil by mouth (1 ounce) and ferric citrate (1½ grains) subcutaneously were then given daily. Seven days later eleven pups (1 dead) were delivered (term of pregnancy 60 days). At that time the dog's red cell count was 6.9 million, and the hæmoglobin 56 per cent. The mother was permitted to nurse 7 pups and the cod liver oil and iron therapy was continued. Ten days after parturition the red cells fell to 5.8 million and the hæmoglobin rose to 69 per cent. The therapy was then discontinued and 19 days later (5 pups nursing, 2 having died) the red cells were 5.4 million and the hæmoglobin 54 per cent. Therapy was resumed. Three weeks later the red cells were 6.0 million and the hæmoglobin 64 per cent. The pups were removed and the therapy was continued, but at the present time, 6 weeks later, her red cells are only 4.4 million and hæmoglobin 70 per cent. (We shall now give her liver extract, since it appeared above as if liver extract stimulated red cell production but not hæmoglobin.)

Dog 26 was operated upon July 2, 1930, and a pouch of the entire stomach was produced. Two months later (September 2, 1930) the red cells were 6.8 million and the hæmoglobin 102 per cent. She copulated and conceived at this time. Three weeks later the red cells were 5.8 million and hæmoglobin 83 per cent. On the fifty-eighth day of pregnancy, the red cells were 4.0 million and the hæmoglobin 66 per cent. The next day parturition occurred. Twelve pups were born, all dying the following week. One week after parturition the red cell count was 6.6 million and the hæmoglobin 73 per cent; one month later the red cells were 6.7 million and hæmoglobin

[1]Lilly's No. 343.

[2]Lilly's No. 343.

81 per cent. Three months after parturition (January 24, 1930) the red cell count is 7.1 million and hæmoglobin 90 per cent. No treatment was given.

Dog 27 was operated July 14, 1930, and a pouch of the entire stomach was produced. Four months later (November 19, 1930) with a red cell count of 7.5 million and a hæmoglobin of 82 per cent, the animal copulated and conceived. Six weeks later anæmia was detected, the red cells being 5.3 million and hæmoglobin 72 per cent. At 7 weeks the red cells were 4.9 million and the hæmoglobin 61 per cent. On January 18, 60 days after copulation, the dog was quite weak but continued to eat normally. The blood picture had not changed. The term of pregnancy was up. Three days later she was very weak, but not too weak to stand and eat. The next day she could not stand. The red cell count was 3.0 million, the hæmoglobin 60 per cent, and the color index 1.2. The dog being overdue and very weak, 200 cubic centimeters of whole blood was transfused and 2 hours later a Porro section was performed. The delivered pups were all alive and appeared to be about 1 week premature. They could not crawl. The following day the red cell count was 4.9 million and the hæmoglobin 78 per cent. Dog died March 13, 1931; grave anæmia; medulla of femur entirely filled with red bone marrow. Histological findings to be reported elsewhere.

Pregnancy has no such effect on normal dogs fed the diet received by our gastrectomized dogs. The chief change in the differential leucocyte count is a monocytosis. We have made no examinations of the duodenal flora of our animals. The stools are negative for parasites.[1]

These results show conclusively that in the presence of experimental achylia gastrica, the additional strain of pregnancy on the organism induces an anæmia that is secondary in type.

DISCUSSION

The stomach has been removed completely or almost completely in dogs or cats by a number of investigators. (Carvallo and Pachon, Monari, Grohé, Fremont—pouch of the entire stomach—and Dagaew.) Czerny and Kaiser had a dog survive five years. Carvallo and Pachon's cat and Dagaew's dog were complete gastrectomies, while in the others some portion of the stomach remained which pouched into a bag. Carrel, Meyer and Levene studied the nitrogen metabolism of 2 dogs, one being completely gastrectomized and the other practically so. Both animals were killed after 3 months, the exact time not being recorded. Mann has recently reported briefly on 3 dogs with total gastrectomy which survived 4 years. None of these observers has reported the occurrence of anæmia. This is not surprising in view of the fact that a spontaneous anæmia has occurred in only 3 of our 14 dogs. Further, the 3 dogs which have developed spontaneous anæmia had a pouch of the entire stomach, and it is possible that the continued drain of gastric juice to the outside was the cause of the anæmia. However, this possibility does not apply to the anæmia of pregnancy in our dogs, since in 1 of the 3 dogs observed, the stomach was removed from the body.

Leake and Ritchie produced an atrophic gastritis in dogs with sodium fluoride and observed the development of an anæmia within 10 weeks. One cannot be certain, however, that the anæmia was not due to the absorption of the sodium fluoride.

Anæmia has been reported to occur after total gastrectomy in man. Hurst (33) states that he knows of 5 cases of total gastrectomy that have developed an Addison's anæmia, but does not give references. As far as we can find, he had in mind 3 cases cited him by Dr. J. R. Bell which were operated for cancer in Vienna, the case of Moynihan, and the case of Hartman (W. F. Mayo). Moynihan's case is not to be questioned so far as anæmia is concerned. His patient died of a grave anæmia 3 years and 8 months after total gastrectomy and autopsy revealed no recurrence of carcinoma. Hartman's case lived almost 3 years after operation and presented a picture simulating pernicious anæmia, but autopsy was not done. Ellis cites a case of gastrectomy for carcinoma which later developed the picture of combined degeneration of the cord and pernicious anæmia, but autopsy report is wanting. Cohn has reported a case of total gastrectomy removed for carcinoma who, 1 year later, developed an anæmia which he maintained was not due to the recurrence of the cancer. A further report is not available. Dennig has reported a case of total resection of the stomach for ulcer which, 8 years later, developed pernicious anæmia. Hochrein has

[1] We desire to express our thanks to Dr. H. R. Fishback of the Department of Pathology for making the stool examinations on our dogs.

reported 2 cases of subtotal gastric resections, 1 for carcinoma which developed typical pernicious anæmia 8 years later and returned to work after receiving liver therapy, and a second which developed an anæmia simulating pernicious anæmia 9 years after subtotal gastric resection for ulcer of the stomach and duodenum which improved on liver and iron therapy. Scheidel has recently reported another case of typical pernicious anæmia developing 6 years after extensive gastric resection for ulcer which responded to liver therapy. Such evidence is very interesting, but its interpretation is open to question.

Anæmia has also been reported to occur after gastro-enterostomy—Campbell and Conybeare, Wilcox, and Delore. Obviously such cases may be due to a coincidence because of the small number of cases in relation to the large number of gastro-enterostomies performed.

The fact that achlorhydria may precede pernicious anæmia by an interval of from 3 months to 25 or more years has been reported by at least 18 authors in the clinical literature. Hurst (34) in 1925 collected 13 cases, in 1930 Conner collected 21, and Davis and Vanderhoof recently reported that they were able to collect 32 cases and had 10 cases of their own, but do not give their references. We have been able to collect 36 cases from the literature: Faber and Gram, 4 cases; Levine and Ladd, 3 cases; Wilkinson, 2 cases; Bie; Cobet and Moravitz; C. Hunter (31); F. Weinberg; Sturtevant; Thaysen; Queckenstedt; Naegeli; Schauman; 1 case each. Kuttner, Riley, Lichty, and Conner, 2 cases each; and Davis and Vanderhoof 10 cases. Riley, in addition to the 2 reported cases, made the statement that he had seen others. In a recent review of the hereditary aspect of achlorhydria in pernicious anæmia, Conner cites 37 authors reporting on a total of 110 families, most of the reports being made since Hurst emphasized the question in 1922. Conner examined 154 blood relatives of 109 patients having pernicious anæmia, and obtained results that confirmed the general belief expressed in the literature; namely, that although "the results do not prove an hereditary aspect of pernicious anæmia, they strongly suggest a familial tendency to the development of one of its most important features," achlorhydria.

The relation of achylia to the etiology of pernicious anæmia has been particularly emphasized by the recent work of Castle, who has demonstrated that if meat is permitted to digest in the stomach of a normal person and is then introduced into the stomach of a pernicious anæmia patient, the blood picture is improved. One of us (Ivy, 36) has pointed out that gastric digestion increases the secretagogue value of food, and that there may be a relation between the secretagogue value of a digest and the anti-pernicious anæmia factor is strongly suggested by the fact that liver and liver extract have a higher secretagogue value than any other known food material (Ivy and Kim, 39).

Many authors have reported on the occurrence of the association of achlorhydria with various forms of secondary anæmia (19, 20). Witts has recently reviewed the literature and has written an extensive article on a condition which he terms "simple achlorhydric anæmia." He defines the condition as a form of anæmia which is not uncommon in women and which occurs occasionally in men, being most frequent in middle and later life. This anæmia is improved by iron therapy. On the other hand, it is well known that secondary anæmia may occur in the presence of normal gastric function.

Three types of anæmia are reported to occur in pregnancy, the pernicious type, the severe hæmolytic type, and the so called "physiologic anæmia" (22, 24, 29, 52, 55).

It is interesting in this connection that the first papers on pernicious anæmia (Channing and Biermers) dealt largely with pregnant cases. In the pernicious and hæmolytic types of anæmia of pregnancy, achlorhydria is frequently reported; however, it is not absolute. Unfortunately, gastric analysis is rarely recorded. Smith reported 8 cases with achlorhydria. Hoskin and Cadle reported another case. Rowland reported 2 cases, but recorded gastric analysis in only 1, which had free acid present. In the studies on the so called "physiologic anæmia" of pregnancy, practically no attention has been given to the stomach. A very recent article by Wills and Mehta contains

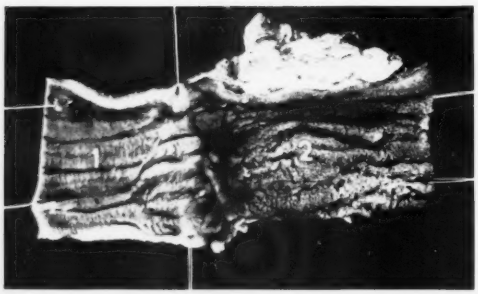

Fig. 1. This figure shows the end-to-end duodeno-œsophageal anastomosis in Dog 1 dying 8 weeks after the operation, of anæmia. *1*, œsophagus; *2*, duodenum.

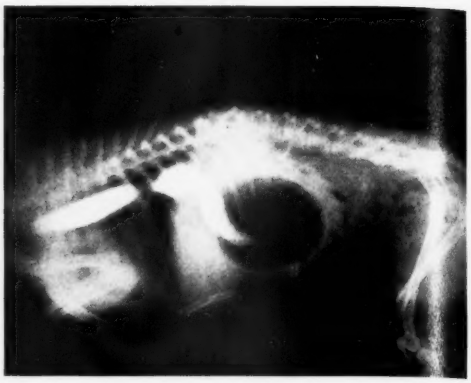

Fig. 2. This roentgenogram shows the end-to-end duodeno-œsophageal anastomosis of Dog 1 shortly before death. No dilatation of œsophagus or duodenum is present. The dark circular air bubble is a balloon filled with air in the "pouch of the entire stomach."

gastric analyses on 50 cases of anæmia of pregnancy. Achlorhydria, however, was found in only a small number. From the available literature on the anæmia of pregnancy, one is led to conclude that anæmia may occur with or without achlorhydria.

As has been pointed out by Sahli and others, it is reasonable to expect that an anæmia may develop in the presence of achlorhydria, since iron salts are insoluble in alkaline solution, and the secretion of gastric juice maintains a slightly acid reaction in the upper intestine which would favor the solution and absorption of iron. If this possibility is physiologically significant, one should expect very little effect from oral iron therapy in achlorhydria. We failed to find an appreciable effect. In order to obtain an evident effect from iron therapy, we had to give it subcutaneously. Nevertheless, there must exist some absorption of iron in our achylic dogs, since they all do not develop anæmia and 1 dog (Dog 10) has maintained a normal hæmoglobin value for over 5 years.

Our interpretation of the anæmia that developed in our dogs is as follows: The digestion of the gastrectomized animal is subnormal, but is adequate under ordinary conditions to insure sufficient digestion and absorption of hæmoglobin and red cell building substances. When some extra demand of the body for hæmoglobin and red cell building substances occurs, or when some cause enters and reduces the already subnormal state of digestion below that minimally required, anæmia results. It is well known that the factor of safety in digestion is large, that total removal of the external secretion of the pancreas more than abolishes the factor of safety, that total continued drainage of bile leads to nutritional disturbances, and that excision of the major portion of the small intestine does the same thing. The excision of the stomach or achylia just about annuls the factor of safety in digestion, we believe. In our dogs the addition of the cod liver oil and iron subcutaneously met the extra demand and substituted for the reduced factor of safety. From our observations on pregnant dogs, anæmia occurring five times in five pregnancies, pregnancy creates an extraordinary demand for red cell and hæmoglobin building substances and places an extra strain on the factor of safety of digestion. Thus, we hold that achlorhydria is a predisposing factor in the genesis of anæmia (32).

We believe that this explanation is applicable to the clinically observed effects of achlorhydria in man. A patient may have an achlorhydria without anæmia because his factor of safety in digestion is adequate and may continue so until some extra demand, strain, or factor enters the picture. This extra demand may be variable such as a Bothriocephalus worm (19, 35), an abnormal duodenal flora with absorption of toxins (12, 19, 34, 41, 60, 65), chronic biliary (40) or pancreatic disease, atrophy of the intestinal mucosa (19), partial chronic intestinal obstruction (19, 47, 59),

Fig. 3. This roentgenogram shows the end-to-end duodeno-œsophageal anastomosis of Dog 3 taken 4 years after the operation and now alive more than 6 years. *1*, œsophagus; *2*, duodenum. Very slight dilatation of œsophagus and duodenum, if any, is present.

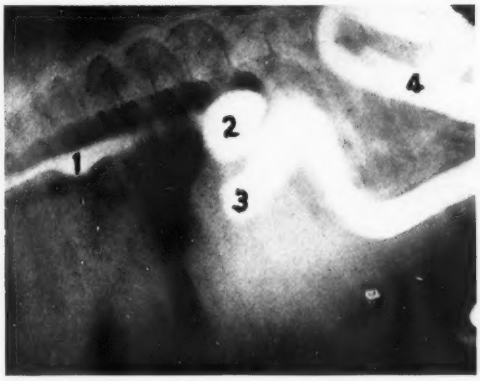

Fig. 4. This roentgenogram shows the end-to-side œsophagoduodenal anastomosis in Dog 16, 2 years after operation. *1*, œsophagus; *2*, œsophagus just above anastomosis; *3*, the start or "blind end" of the duodenum; *4*, the jejunum. There is no dilatation of the duodenum and very slight, if any, dilatation of the lower end of the œsophagus.

pregnancy, etc. This view is compatible with the fact that anæmia may occur in the absence of achlorhydria (omitting anæmias due to specific dietary deficiency), since the extra demand may outweigh the factor of safety in digestion.

SUMMARY

Gastrectomized dogs when properly fed maintain themselves surprisingly well. A spontaneous secondary anæmia has developed in 3 of 14 dogs with absolute achylia gastrica on a diet adequate for normal dogs. Pregnancy has uniformly induced an anæmia (3 times in 1 dog, 1 time in each of 2 dogs). The anæmia can be controlled by cod liver oil by mouth and iron subcutaneously. We believe that the achlorhydria is a predisposing factor for the development of anæmia in that it reduces the factor of safety of digestion. Other observations on the effect of withdrawal of the functions of the stomach are reported.

Fig. 5. This roentgenogram shows the end-to-end duodeno-œsophageal anastomosis in Dog 11, 2 years after operation. *1*, œsophagus; *2*, duodenum. No dilatation is present.

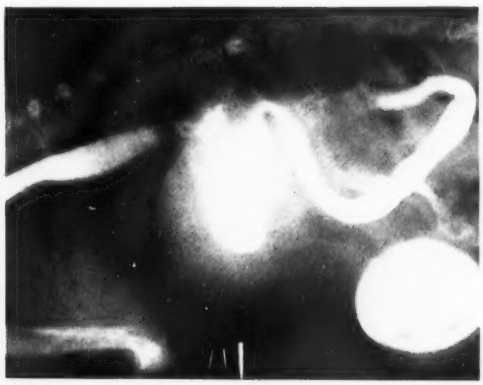

Fig. 6. This roentgenogram shows the end-to-side œsophagoduodenal anastomosis in Dog 27, 6 months after it had been operated upon. No dilatation was present at this time.

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THE PEPTIC GENESIS OF GASTRIC AND DUODENAL ULCER

Especially in the Light of Ulcers in Meckel's Diverticulum and the Postoperative Ulcers in the Jejunum[1]

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THE research work of recent years has in many respects brought about a fundamental alteration of our views on the pathogenesis of gastric and duodenal ulcer. Thus, the old theory, put forward by Virchow and further developed in 1926 by Hauser, that anatomical changes in the vessels attended by mucosal infarcts are the cause of gastric and duodenal ulcer and as well, the hypothesis framed on clinical grounds by von Bergmann in 1913, that the ulcers may be attributed to a neurogenic spasm of the vascular or gastric walls, have both been generally rejected.

Broadly speaking, it has not been possible by histological examination to disclose evidence of any primary alteration of the vessels, nor has it been possible to establish any definite relation between vascular distribution and ulcer location. Moreover, the study of the ulcer complex has brought to light a series of facts for which these two vascular theories fail to provide any satisfactory explanation. In seeking for the underlying cause of ulcer, it has been ascribed to a great variety of conditions, among which might be mentioned: bad dietary habits, lack of vitamins, food idiosyncrasies, focal infections of the mouth, tonsils, and appendix, specific streptococci, smoking, overwork, and so on. This obviously shows the need of further investigation in the genesis of ulcer.

ULCER GASTRITIS—ANATOMICAL PICTURE AND ETIOLOGY

Undoubtedly the most important observation made of late years is the regular appearance in ulcer cases, of a gastritis-like change confined to the pyloric portion of the stomach (Moszkowicz, Konjetzny and co-workers, Buechner, and in the Scandinavian countries, Wimtrup, Nicolaysen, Bjarne Dahl, Kalima, Bohmansson, Ringertz). The pioneer work was here performed by Konjetzny and his collaborators, who have given an exhaustive account of the histological aspect, have pointed out the constant occurrence (up to 100 per cent) of these gastritic changes, and have demonstrated a relationship between them and the fully developed ulcer. Hitherto, as far as literature shows, rather little attention has been paid to these findings in England and the United States.

The histological gastritic picture is rather similarly described by all the investigators.

At the pathological institute in Lund, Ringertz has made a critical review of the question of the anatomical picture underlying ulcer gastritis. Like other observers, he finds these gastritic changes constant, and localized to the zone of pyloric glands, or to the duodenum. In two-thirds of the cases the changes are of a chronic type. Hypertrophic, hypertropho-atrophic, or atrophic mucous membrane changes may be present. There is also a considerable cellular infiltration between the glands, and in about 50 per cent of the cases there is a pronounced hyperplasia of the follicular apparatus (so called gastritis follicularis) localized at the pyloric end. In addition to the chronic inflammation, a small number of cases have an acute irritation, especially striking on account of leucocytic infiltration. Not infrequently this infiltration is confined to the intermediate layer of mucosa, on a level with the gland necks, a fact that has been interpreted by Ringertz as indicating that the juvenile cells within this center of proliferation are especially sensitive to the injurious agent. A duodenitis analogous to this is likewise described, though the changes here do not, for the most part, attain the same degree of development as in the pyloric end of the stomach. The difference that

Fig. 1. Schematic diagram of the gland areas (from Buechner). *C*, Cardiac, *F*, fundic, and *P*, pyloric glands.

[1]From the Pathological Institute, University of Lund, Sweden.

Fig. 2. Normal stomach slit along the greater curvature. The borderline between the fundic and pyloric gland zones is marked by a dotted line.

appears to exist when a comparison is made between ulcer cases from different clinics manifests itself chiefly in the varying frequency of the acute gastritic changes and erosions. Ringertz considers that these differences are due to variations in the acidity conditions at the different places, and that they also depend upon the phase (exacerbation or remission) under which gastrectomy is performed.

In the very earliest stage, that preceding the formation of erosions, Buechner has been able to prove the presence in man of a fibrinoid necrosis, which is subsequently digested by the gastric juice, leaving an erosion. In his experiments on animals, described later on, in which he produced ulcers by pouring hydrochloric acid into the stomach and by other means, Buechner has encountered the same fibrinoid necrosis in the earliest phase of the lesions.

That these changes in the mucosa are not secondary conditions of irritation in the tissues surrounding the ulcer, but primary to or parallel with the initial stage of ulceration, is shown by the fact that the gastritis is uniformly pronounced over the entire pyloric end irrespective of the site of the ulcer (e.g., in the duodenum) and by the fact that this type of gastritis (with clinical symptoms of ulcer) also occurs in cases without any ulcer (Konjetzny, Bjarne Dahl).

The question of prime importance is now: *What is the etiology of these changes in the mucous membrane and how is their development to be conceived?*

The Kieler school supplies only a very meager answer to these questions. Konjetzny and his collaborators attribute the changes to an ordinary exogenous gastritis produced by mechanical, chemical, or thermal irritants, while bacterial etiology is not considered to come into the question. Of special interest is the fact that they totally deny the possibility of the acid gastric juice being the primary causal factor and regard the current designation "peptic ulcer" as misleading and erroneous.

This view held by the Kieler school obviously possesses several weak points and overlooks too many physiological factors. For instance, no explanation is given of the localization of the gastritis to the pyloric end. This ulcer gastritis, however, presents such distinctive features that it can scarcely be denoted as an ordinary gastritis. Its often extremely chronic course, with recurrences not uncommonly appearing for decades, argues far more in favor of a deeply rooted constitutional cause which is inherent in the individual himself.

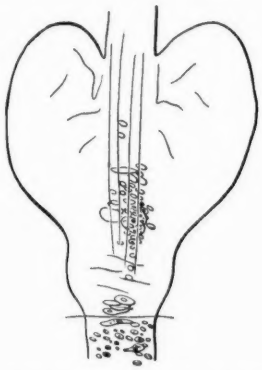

Fig. 3. Diagram recording the sites of a large number of gastroduodenal ulcers observed by Orator.

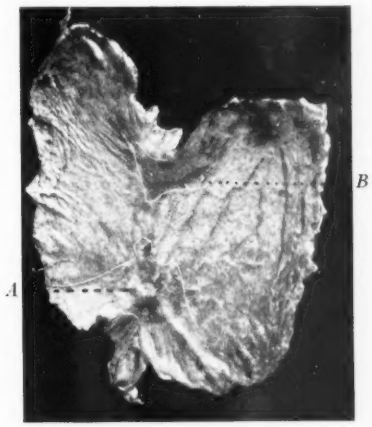

Fig. 4. Chronic gastric ulcer situated in the zone of cardiac glands, distinguished by its darker color. In addition a pyloric ulcer. *A*, Pyloric ulcer; *B*, cardiac ulcer.

All this would tend to show that it is to the biochemical conditions (the acid gastric juice) that we have to look for the primary cause of the typical gastric and duodenal ulcer.

This view, which was plainly put forward by Guenzburg as far back as 1852, has ever since then played a more or less prominent part in the discussion of ulcer etiology and has found expression in the clinical designation, peptic ulcer (Quincke, 1879).

After having been eclipsed for a time, especially in Germany, by Virchow-Hauser's and von Bergmann's theories, the biochemical view of ulcer genesis has again attracted lively attention. Principally because of the work of Buechner and his collaborators in this field, a more complete and consistent development of the doctrine postulating the importance of peptic injuries to the mucous membrane has resulted.

The aforementioned investigators, e.g., Virchow, Hauser, and von Bergmann, also saw in the gastric juice an active factor in the development of ulcers, though one that only acted on a membrane which was injured or dead through infarction. In like manner the gastric juice had an influence on the maintenance and enlargement of the ulcer. The living and uninjured mucosa, on the other hand, was considered to possess a natural quality which protected it against injury from its own secretion.

ANATOMY AND PHYSIOLOGY OF THE GASTRAL SYSTEM AND THE POSITION OF ULCERS

Our understanding of the primary injuries to the mucous membranes by the acid gastric juice is due to increased knowledge of the various histologically and biologically heterogeneous zones of glands in the stomach (Oshikawa, Moszkowicz, Zimmermann, Stoehr, Orator, et al). From the standpoint of anatomy and physiology the upper portion of the duodenum also belongs here, and for all these parts of the digestive canal Aschoff has found "gastral system" a suitable term. Counting from the œsophagus the following zones come in turn (see Fig. 1): (1) The narrow zone of cardiac glands (ordinarily 1.5 centimeters in breadth); (2) the zone of fundus glands; (3) the zone of pyloric glands; and (4) the duodenal mucous membrane.

It is especially to be noted that the zone of pyloric glands on the lesser curvature reaches considerably higher up (above the angulus) than on the greater curvature (see Fig. 1). On slitting the stomach along the greater curvature the borderline between the fundus and pyloric gland zones runs as indicated in Figure 2.

This transition is not particularly sharp, there being a zone a few millimeters in breadth where glands of both types are mixed together

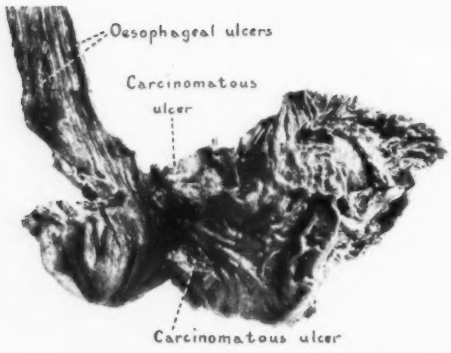

Fig. 5. Hour-glass stomach (carcinomatous ulcer cut across) with two oblong peptic ulcers in the lower œsophageal region.

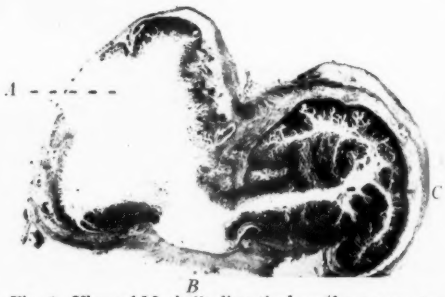

Fig. 6. Ulcer of Meckel's diverticulum (from a specimen of Dr. Buechner's Case 2). *A*, Ileum; *B*, callous ulcer situated in ordinary intestinal mucosa at the neck of the pouch; *C*, Meckel's diverticulum lined by hyperplastic mucosa of fundic type.

and which is usually called the intermediate gland zone.

The fundus gland area differs from the other portions by the presence of the characteristic glands containing chief and parietal cells and constitutes the sole source for the production of hydrochloric acid and pepsin.

No such secretion takes place in the other glandular zones; here there is a production of slightly alkaline or neutral mucus. The mucous membrane of the pyloric glands, however, exercises a regulative action on the production of gastric juice from the fundus. Stimulation is evoked by food, while the acid mixed chyme, on coming into contact with the mucosa of the pyloric glands, has an inhibitory action on this secretion.

The central point in Buechner's representation is, now, that *ulcers arise in the areas of activity of the gastric juice, whereas the area of production possesses by nature a relatively high power of resistance.*

This receives strong support from the careful record made at various clinics of the position of ulcers in a large number of cases. A good instance of this is afforded by Figure 3, which has been taken from Orator.

It is then seen that exceedingly few ulcers are located within the area of the fundus glands, these lesions being mostly in the form of radiate scars and not of the callous type, while the sites of election are to be found either in the area of the pyloric glands, and then especially at the upper angle in the vicinity of the angulus where the opportunities for acid action are manifestly greatest, or in the proximal part of the duodenum, particularly close to the pylorus.

Occasionally ulcers are encountered in the area of the cardiac glands (in about 5 per cent of the cases) though not marked in Orator's diagram (Fig. 3). In the autopsy material of the Institute we have met with ulcers in this region several times. In one case, illustrated in Figure 4, we observed that the ulcer was situated in the cardiac area, marked off from the surrounding mucosa by its color, and showing cardiac glands microscopically.

Should the gastric juice have an opportunity of acting upon the mucous membrane of the œsophagus, ulcers could also originate there. A predisposing factor is stagnation of the stomach contents, e.g., in hour-glass stomach. In one of our own cases (Fig. 5) it could be seen by fluoroscopy that there was an insufficiency of the cardiac sphincter and that the contents of the stomach perpetually regurgitated up into the lower œsophagus, the subsequent autopsy disclosing two oblong ulcers here (as well as an hour-glass stomach due to ulcer carcinoma).

Another instance of this law of localization is afforded by the postoperative jejunal ulcers, in which the lesion is invariably located within the area of the intestinal mucous membrane and usually close up against the gastroenterostomy (this phase of the subject is discussed more fully elsewhere in this article).

Lastly, in cases of Meckel's diverticulum with a heterotopic gastric mucosa we find in a not inconsiderable number of instances chronic ulcers likewise situated within the area of the intestinal mucous membrane. This interesting chapter will be referred to more fully later on.

THE IMPORTANCE OF AN EXCESS OF ACID GASTRIC JUICE

The feature common to all these cases is the accessibility of the respective areas to the action of hydrochloric acid.

In ulcer disease, normal or hypernormal values of hydrochloric acid are found, whereas a low acid figure or achlorhydria is rare. Below are given the acid levels found by Kalk at von Bergmann's clinic and by Hurst and Stewart in London hospitals.

Kalk	Gastric Ulcer per cent	Duodenal Ulcer per cent
Anacidity	4	0
Subacidity	15	0
Normacidity	52	25
Superacidity	29	75

Hurst and Stewart	Gastric Ulcer per cent	Duodenal Ulcer per cent
Anacidity	1.9	0
Subacidity	7.6	0
Normacidity	58.4	39.0
Superacidity	32.1	61.0

To earlier ulcer statistics indicating higher percentages of anacidity, cannot be attributed decisive value, as they belong to the time preceding the introduction of fractional gastric analysis and of the histamine test. Low acidity after a test meal does not necessarily indicate slow secretion of gastric juice because the acid may be partly neutralized by the alkaline duodenal juices. It should also be remembered that in the case of old ulcers, an anacid finding tells us nothing about the acid conditions prevailing at the time the lesion originated. Kalk says: "Es gibt kein frisches Ulcus pepticum in einem anaciden Magenmilieu." It is also an interesting fact that in pernicious anæmia, practically all of which patients present a true achylia, neither acute nor chronic ulcers have ever been observed as a complication.

Our knowledge of the conditions under which an excess of hydrochloric acid makes itself felt is rather insufficient. A long time ago Pavlov suggested that the gastric juice as it flows from the gastric glands possesses a constant acidity. Quite recently Hollander and Cowgill have confirmed this by collecting in experimental animals the secretion from isolated gastric pouches without any irritation or contamination. They report that the value of the maximum acidity in hydrogen ion units was 0.91 ± 0.02 (0.55 per cent hydrochloric acid) and that variations in the rate of secretion were not of necessity associated with corresponding changes in acidity.

From this it follows that hypersecretion is brought about, not by concentration of the gastric juice, but by production of a larger volume of fluid. Accordingly it has been suggested[1] to drop the word "hyperacidity" from clinical nomenclature.

An excess of hydrochloric acid may be ascribed to three factors: (1) supersecretion, (2) failure of reduction or neutralization of the gastric juice, and (3) lowered resistance of the gastro-intestinal wall. These three factors may act alone or side by side in the different cases. Briefly summed up they are:

1. A supersecretion of nervous origin (von Bergmann: "Dysharmonien im vegetativen Nervensystem") and not infrequently in connection with psychic influences (Pavlov). The occurrence of ulcers in association with brain affections (Haudeck) or after an operation for cerebellar tumor (Cushing, 3 cases) also indicates the possibility of central incitation of increased acid secretion. In these cases, however, the effect of the additional factor of the stomach being empty must be taken into account.

To this same group belong the cases in which unsuitable food is the cause of supersecretion, as in Bergsma's observation. He noticed a very high frequency of gastric and duodenal ulcers among the natives of Abyssinia, in contrast to the Negroes in that country. The most obvious difference was in diet. The natives eat daily a dish with a sauce that is approximately 50 per cent cayenne pepper.

2. Unsatisfactory activity of the protective measures at the disposal of the organism against high acid value. Rather little attention has hitherto been paid to this part of the

[1] J. Am. M. Ass., 1931, xcvi, No. 26.

problem, compared with the intense study of supersecretion. According to Kalk the following processes act as protective measures: (a) The diluent reaction that comes into operation when a certain hydrogen ion concentration is reached; (b) the inhibited production of hydrochloric acid when the stomach is at rest; (c) the production of mucus by the gastric mucous membrane, thus forming a mechanical protection for the mucosa; (d) neutralization through the regurgitation of the alkaline duodenal contents.

One or several of these protective measures might fail and an excess of hydrochloric acid arise.

3. A lowered resistance of the gastro-intestinal wall, caused perhaps by general disturbances of the circulation (Buechner) or reduced local blood supply (Kalk).

It is evident that these problems derive little or no help from a patho-anatomical investigation of the material. To cover all these functional disturbances in the motility, the secretion, and the blood supply of the stomach, von Bergmann has coined the expression "Dysharmonien im vegetativen Nervensystem."

EXPERIENCE FROM ANIMAL EXPERIMENTATION (BUECHNER)

In their study of the gastric juice as cause of the peptic lesions, Buechner and his coworkers have carried out a series of supplementary experiments under diverse conditions. Only a brief account of these most interesting experiments can be given here; for further particulars the reader is referred to Buechner's exhaustive account.[1]

Artificial erosion by hydrochloric acid. By pouring 0.8 to 1.5 per cent hydrochloric acid into the stomach of cats it was possible to produce an erosive gastritis with gross and minute circumscribed defects of the substance. The histological picture accords in all details with that in acute peptic gastroduodenitis.

Histamine ulcers in rats. By hypodermic injections of histamine, which is our most potent pharmacological agent for stimulating the production of gastric juice, it was possible to cause ulcers in the rumen or œsophageal portion of the stomach of rats. Particularly regular was the appearance of these ulcers in the empty stomachs of fasting animals. These experiments provide a means of accounting for the presence of ulcers in burns, a combination that has long been known (Curling's ulcer) although its pathogenesis has been extremely puzzling. It has been demonstrated (Kaufmann) that histaminoid products are formed in burns. A resulting rise in the hydrochloric acid level in conjunction with an empty stomach obviously furnishes, in the light of the experimentally produced histamine ulcers, a sufficient explanation of the gastric and duodenal ulcers found in association with injuries from burns.

Operatively produced excess of hydrochloric acid. For some time von Eiselsberg's "Exclusio pylori" was used in the surgical treatment of ulcers. This method, however, was rather quickly abandoned, as it developed that peptic jejunal ulcers appeared rather often as a complication; according to some investigators, in 20 to 30 per cent of the cases. Increased acid production and absence of neutralization by the contents of the duodenum were responsible for this situation. Similarly, in surgical experiments on animals, by incapacitating the physiological neutralizing power of the duodenal juices, several investigators have succeeded in producing an excess of hydrochloric acid and constant ulcer formation (Mann and Williamson, Morton and Graham).

Ulcers by sham feeding. By repeating Silbermann's sham feeding experiments on dogs over a considerable time, acute peptic changes with ulcer formation in the stomach and duodenum were obtained. In these experiments, too, there is the ulcer favoring combination of increased acid production and an empty stomach.

In all these experiments, the absolute or relative excess of hydrochloric acid constitutes the common factor in the origin of ulcer, a fact that lends weighty support to Buechner's view of the genesis of this disease. To this must be added the fact that the histological picture of these experimental ulcers agrees on all essential points, with corresponding acute changes in man.

[1] Die Pathogenese der peptischen Veraenderungen. Jena: Gustav Fischer, 1931.

This view of the action of the gastric juice on the previously discussed portions of the mucous membrane, marked by a diffuse gastroduodenitis, is apparently in contradiction to the well known experience that the developed ulcers only attain a limited size and are commonly not multiple.

Here a number of factors are at work. The folds of the mucosa obviously cause certain circumscribed areas to be more exposed to the gastric juice, with the result that the primary defects will be unequal in size. These multiple erosions, however, may be reduced and protected by contractions of the muscularis mucosæ, and thereby healed. A damaged or perforated muscularis mucosæ is unanimously considered to be of great significance. The protecting contraction does not then supervene and the muscularis mucosæ draws upon the defect instead and enlarges it. A further obstruction to healing is obviously the position of a lesion in the gastric pathway (Magenstrasse) or at narrow passages, where functional factors may mechanically contribute to the chronicity of the ulcer (Aschoff). To these must be added the continued action of hydrochloric acid in the base of the ulcer.

The value of the evidence in the ulcer producing experiments described is limited, however, on account of the fact that the lesions were produced in animals, and under conditions that considerably diverge from the physiological. Of so much greater value, on the other hand, are some experiences from human material.

EXPERIENCE FROM HUMAN MATERIAL

Under ordinary conditions, a typical peptic ulcer never occurs in the intestinal canal below the common outlet of the bile and pancreatic ducts. Only in those cases in which the gastric juice has an opportunity of acting directly upon the mucous membrane of the small bowel does one encounter ulcers of a typical character in that region. Such circumstances exist after a gastro-enterostomy when the jejunal mucosa adjoins the gastric mucosa and in certain cases of Meckel's diverticulum when the intestinal mucous membrane is interspersed with heterotopic mucosa of a fundic type.

This latter observation may, in fact, be regarded as a model experiment of nature[1] demonstrating the pathogenesis of ulcer. It affords one of the best supports for Buechner's view.

ULCER IN MECKEL'S DIVERTICULUM, CLINICAL AND ANATOMICAL PICTURE

With reference to ulcer formation in Meckel's diverticulum, Konjetzny states: "Dass die Geschwuere in Mechelschen Divertikel ohne weiteres als 'peptisch' bezeichnet werden, nur weil im Grunde des Divertikels Magenschleimhaut nachzuweisen ist, ist nach meiner Ansicht eine von den vielen unbewiesenen Behauptungen a priori, die bei kritischen Betrachtung nicht gerade stichhaltig sich erweisen." Konjetzny thinks that if the dystopic gastric mucosa in the top of the diverticulum really produces any pepsin and hydrochloric acid at all, this product would be immediately neutralized by the alkaline intestinal juice.

With reference to Konjetzny's statement and in annotation of some personally observed cases, it appears justifiable to give here a somewhat more detailed account of this hitherto rather unnoticed ulcer location,[2] especially as in Buechner's latest publication (1931) only some 15 cases from the literature are reported and it has proved possible to more than double this figure. To save space the cases from the literature are briefly summarized in Table I.

In addition to the cases which are summarized in Table I, and in which the presence of gastric mucosa has been verified microscopically, there is in the literature another group of similar cases in which the mucosal histology was not investigated. The macroscopic operative or autopsy findings of a typical ulcer, however, together with the clinical picture (intestinal hæmorrhages, pains) so completely resemble those of the cases recorded in the table that we can consider them together.

[1] Quite recently Warren B. Matthews (Proc. Soc. Exper. Biol. & Med., 1931, xxviii, No. 9) has attempted to duplicate this situation experimentally by making a small Pavlov pouch and causing it to empty into an isolated loop of lower ileum. In all his 6 dogs large ulcers (from 1 to 5 centimeters across) were formed in the ileal mucosa adjacent to the gastric pouch. The ulcers were chronic in type and found between 30 and 80 days. Two of the dogs died of peritonitis from perforation of ulcers.

[2] This article was almost finished before the excellent paper of Aschner and Karelitz (Ann. Surg., 1930, xci) came into our hands.

CASES OF ULCER IN MECKEL'S DIVERTICULUM WITH MICROSCOPICALLY VERIFIED GASTRIC MUCOSA

Author Publication	Age Sex	Symptoms			Pathological examination		Note
		Pains	Hæmorrhage or anæmia	Perforation	Location of ulcer	Type of ulcer	
1. Hilgenreiner. 1903 (23)	18 male	Several years severe abdominal pains, especially in connection with meals	Repeated intestinal hæmorrhages	——	At the junction of intestinal and gastric mucosa	Penetrating ulcer, adherent to parietes	Operated upon. Well.
2. Deetz. 1907 (11)	9 male	For 2 days generalized abdominal pains	No intestinal hæmorrhages	Signs of peritonitis	At the neck of Meckel's diverticulum	Perforated ulcer	In addition pancreatic tissue. Operated upon. Well.
3. Huebschmann. 1914 (25)	4½ male	Trauma to abdomen	Two or three intestinal hæmorrhages. Once hæmatemesis	Signs of perforation and peritonitis a month since the abdominal trauma	At neck of Meckel's diverticulum adjacent to the gastric mucosa	Perforated peptic ulcer	Died. Autopsy.
4. Gramén. 1915 (14)	10 male	Slight abdominal pains during a year	During this year a marked anæmia noticed	Signs of peritonitis for 15 hours	At neck of Meckel's diverticulum adjacent to the gastric mucosa	Peptic ulcer	Operated upon. Well.
5. Callender. 1915 (9)	19 mos.	——	Two intestinal hæmorrhages with an interval of 36 hours. The last hæmorrhage was lethal	——	In ileum, at the border on Meckel's diverticulum	Peptic ulcer	Died. Autopsy. Sex not recorded.
6. Meulengracht. 1915 (38)	12 male	For 14 days generalized abdominal pains	Copious intestinal hæmorrhage	——	In Meckel's diverticulum in mucosa of intestinal type	Penetrating peptic ulcer	Died. Autopsy.
7. Mueller. 1919 (42)	11 male	For 14 days pains in the lower part of abdomen	In connection with abdominal colic, black stools	Signs of peritonitis	At the neck of Meckel's diverticulum in ordinary mucosa	Perforated ulcer	Operated upon. Well.
8. Mueller. 1919 (43)	11 male	Symptoms of intestinal obstruction	——	——	In a cyst, found in a cord connecting umbilicus and a Meckel's diverticulum	A recently healed ulcer, without signs of tuberculosis or other special changes	Blood found in the cyst. Operated upon. Well.
9. Mégevand and Dunant. 1922 (36)	28 male	Since birth been suffering from intermittent abdominal pains to a certain extent in relation to meals	Since his first year several black and bloody stools. At last threatening intestinal hæmorrhage	——	At neck of Meckel's diverticulum adjacent to gastric mucosa	Peptic ulcer	Operated upon. Well.
10. Brasser. 1924 (26)	15 male	On one occasion pains in the lower part of abdomen	Ten days later great intestinal hæmorrhages. Marked anæmia	At operation origin of bleeding was not found. 8 days later signs of peritonitis	At neck of Meckel's diverticulum in ordinary mucosa	Perforated peptic ulcer	Died. Autopsy.
11. Humbert. 1924 (26)	11 mos.	For 1 day abdominal pains. Vomiting	At 5 and 8 months of age intestinal hæmorrhages	Signs of peritonitis	Near the apex of Meckel's diverticulum adjacent to gastric mucosa	Peptic perforated ulcer	Died. Autopsy.
12. Guibal. 1924 (17)	14 male	Slight abdominal pains in connection with hæmorrhage	Repeated intestinal hæmorrhages for several months	——	At the neck of Meckel's diverticulum adjacent to gastric mucosa	Chronic penetrating ulcer	Operated upon. Well.
13. Pascale. 1925 (45)	41 female	Many years abdominal pains especially associated with diet faults	Once, several years before operation, a hæmorrhage per rectum	——	In the middle of Meckel's diverticulum a healed perforation	Peptic ulcer	Operated upon. Well.
14. Ulrich. 1925 (55)	8 mos.	——	Intestinal hæmorrhage	Signs of peritonitis	In intestinal mucosa of Meckel's diverticulum	Perforated peptic ulcer	Died. Autopsy.
15. Abt and Strauss. 1926 (1)	2 female	Abdominal cramps for 2 months	In connection with these pains black stools	——	Near the apex of Meckel's diverticulum	Peptic ulcer	Operated upon. Well
16. Buechner. 1927 (27)	24 male	——	——	Signs of peritonitis	At the neck of Meckel's diverticulum in ordinary mucosa	Chronic peptic ulcer	——
17. Kleinschmidt Case 1 1926 (32)	15 male	Abdominal pains for a year, especially 1½ hrs. after meals	About a year ago severe intestinal hæmorrhage	Signs of peritonitis	At the base of Meckel's diverticulum near junction with intestine	Chronic peptic ulcer	Operated upon. Well.
18. Jackson, A. 1927 (28)	14 male	Abdominal cramps for 4 days	On third day copious bright red stools	——	In Meckel's diverticulum adjacent to gastric mucosa	——	Operated upon. Well.

CASES OF ULCER IN MECKEL'S DIVERTICULUM WITH MICROSCOPICALLY VERIFIED GASTRIC MUCOSA—*Continued*

Author Publication	Age Sex	Symptoms			Pathological examination		Note
		Pains	Hæmorrhage or anæmia	Perforation	Location of ulcer	Type of ulcer	
19. Taylor. 1927 (52)	17 mos. male	Diarrhœa	Three great intestinal hæmorrhages in the course of 4 mos.	——	In intestinal epithelium at the line of junction with gastric mucosa	Peptic ulcer. Shallow ulcer, ¼ inch across	Died. Autopsy. The diverticulum situated in the mesenteric wall of the bowel.
20. Gramén. 1927 (15)	11 female	Slight abdominal pains	——	Signs of perforation and peritonitis	——	Peptic ulcer	Operated upon. Well.
21. Gramén. 1927 (15)	21 male	Slight abdominal pains	——	Signs of peritonitis	——	Peptic ulcer	Operated upon. Well.
22. McCalla. 1927 (35)	$3^{10}/_{12}$ male	Slight abdominal pains	Repeated intestinal hæmorrhage since the age of 14 mos.	Signs of perforation and peritonitis	In ileum, adjacent to the diverticulum	Perforated ulcer	Died. Autopsy.
23. Meiss. 1928 (37)	2	At 6 mos. of age generalized abdominal pains. Abdominal cramps for the last 3 weeks	In connection with such pains a very bloody stool on one occasion	——	In Meckel's diverticulum adjacent to gastric mucosa	Peptic ulcer	Operated upon. Well.
24. Franke. 1929 (13)	—	——	——	Signs of peritonitis	In Meckel's diverticulum. In ordinary mucosa	Peptic ulcer	Died.
25. Hartglass. 1928 (20)	4 female	——	——	Signs of peritonitis	At the base of Meckel's diverticulum	Perforated ulcer	Operated upon. Well.
26. Peterman and Seeger. 1928 (46)	6 male	Abdominal pains	Intestinal hæmorrhage. Hæmoperitoneum. Anæmia	Sealed off perforation	At the base of Meckel's diverticulum	Chronic ulcer	Operated upon. Well.
27. Treplin. 1929 (54)	—	Symptoms of an appendicitis appendectomy—abdominal pains again	——	Signs of peritonitis	At the neck of Meckel's diverticulum in ordinary mucosa	Peptic ulcer	Operated upon. Well. Gastric juice verified from a fistula.
28. Winkelbauer. 1929 (58)	19 mos. male	Generalized abdominal pains for some hours. Vomiting	Several great intestinal hæmorrhages. Anæmia	——	In the base of Meckel's diverticulum	Peptic ulcer	Operated upon. Well.
29. v. Haberer. 1930 (18)	13 male	Abdominal cramps Appendectomy. Pains again	Black stools. Marked anæmia	Walled perforation	In Meckel's diverticulum adjacent to gastric mucosa	Chronic peptic ulcer	Operated upon. Well.
30. v. Haberer. 1930 (18)	21 male	Heartburn for 1 to 2 years	Once a great bloody stool	——	In Meckel's diverticulum adjacent to gastric mucosa	Peptic ulcer	Operated upon. Well. In addition two peptic duodenal ulcers.
31. Schmidt. 1930 (50)	18 male	——	——	Signs of peritonitis	Near the neck of Meckel's diverticulum adjacent to gastric mucosa	(a) Peptic ulcer (b) Peptic perfor. ulcer	Operated upon. Well. Two ulcers found.
32. Edwards. 1930 (12)	16 male	Abdominal pains for many years sometimes in connection with meals	Several intestinal hæmorrhages. Anæmia	Signs of peritonitis	Near the base of the diverticulum	Perforated peptic ulcer	Operated upon. Well.
33. Aschner and Karelitz. 1930 Case 1 (2)	15 mos. female	A tender mass in the lower abdomen	Intestinal hæmorrhage. Hæmoglobin 55 per cent	——	In ileum, adjoining the gastric mucosa of the Meckel's diverticulum	Chronic penetrating ulcer	Operated upon. Well.
34. Aschner and Karelitz. 1930 Case 2 (2)	26 mos. male	Abdominal pain in the umbilical area	Passed bright red blood per rectum several times. On one admission hæmoglobin 30 per cent	——	At the neck of Meckel's diverticulum at the junction of intestinal and gastric mucosa	Peptic ulcer	Operated upon. Well.
35. Buechner. 1931 (7)	8 female	For several weeks abdominal cramps in connection with meals. Vomiting	——	——	In ileum at the neck of Meckel's diverticulum	Chronic peptic ulcer	Operated upon. Well.
36. Lindau and Wulff. 1931 Case 1 (See text)	15 male	For several years griping abdominal pains	——	Signs of perforation and peritonitis	At the apex of Meckel's diverticulum in intestinal epithelium close against gastric mucosa	Perforated callous ulcer	Appendectomy. Died. Autopsy.
37. Lindau and Wulff. 1931 Case 2 (See text)	5 female	——	Umbilical hæmorrhages every year	——	In an umbilical pouch partly lined by gastric mucosa	Chronic peptic ulcer	Operated upon. Well.

Such cases have been reported by Denneke (1903); Brentano (1904); Laewen (1909); Griffith (1914); R. H. Jackson (1924); Stulz and Woringer, (1926), 2 cases; Abt and Strauss, case 2 (1926); Moore (1926), 2 cases; Fuss (1926); Kleinschmidt (1926), case 2.

AUTHORS' OWN CASES

CASE 1. Boy of 15 years. For several years patient has been troubled at periods with "griping pains in the stomach," for which he had sometimes been confined to bed; on one occasion for 4 days. On October 20, 1925, at noon, he fell ill with perforation symptoms, followed by developing peritonitis. Operation was done 3 hours later: appendectomy and lavage. The appendix was found only secondarily involved in the outer parietal layers (microscopically verified). Patient died after 48 hours of peritonitis.

Autopsy revealed a purulent, diffuse peritonitis and a Meckel's diverticulum the size of a thumb, with well developed mucous membrane, which did not exhibit any macroscopically distinct inflammatory irritation. At the apex of the diverticulum there was a polypous and flabby area 2 centimeters in diameter. Close against this there was a perforation the size of a pea with even, rounded, and somewhat discolored margins but without any distinct inflammatory reaction from the surrounding mucosa. For the rest, the mucous membrane was swollen with prominent follicles, though without lesions or exudate.

Microscopical examination showed a perforating callous ulcer, seated in an essentially unchanged mucosa of intestinal type. The polypous, circumscribed area of the mucosa had a fundic character, but here postmortem changes prevented closer analysis.

CASE 2. Girl of 5 years. Patient had had a secretory fistula in the umbilical tract since birth. Every year there were occasional hæmorrhages from this fistula, lasting at times half an hour or so. She visited a hospital at Ängelholm because of increased umbilical hæmorrhages. Here an omphalic fistula secreting a thin fluid without urinous odor was discovered.

Operation, including excision of the navel and of a small sac was done. The latter, which was closed toward the peritoneal cavity, was assumed to be the remains of the omphalomesenteric duct. Microscopical examination revealed mucosa of fundic character on a small area and adjoining this a chronic ulcer with reaction from the surrounding connective tissue and apparently the source of the bleeding.

This case agrees in essentials with that described by P. Mueller, 1919 (No. 8 in the Table) and shows that an ulcer may originate even in a fetal rest of the omphalomesenteric duct without connection with the intestine.

As indicated by the tabular cases reported from the literature and by the Lund cases, Meckel's diverticulum is not a particularly rare ulcer locality. It is remarkable that among the authors cited some have seen repeated cases; our countryman, K. Gramén, no fewer than three.

Clinical manifestations. In contrast to the ordinary gastroduodenal ulcer, similar lesions in Meckel's diverticulum appear more especially at early ages. The majority appear before puberty and often even within the first year. The majority of cases occur in male children, as can be seen from the table, only a few cases (7) proving an exception to this rule.

Three main features characterize the clinical aspect: pains, intestinal hæmorrhages, and symptoms of perforation.

The pains may at times be entirely absent or of short duration. As a rule, however, the cases show more or less pronounced attacks of pain, not infrequently of periodic recurrence, at times in association with meals. In Cases 9 and 13 in which ulcer in Meckel's diverticula occurred at adult ages, these attacks had an ultrachronic character. In other cases, pains were a signal of the starting of perforation.

Repeated intestinal hæmorrhages form the most constant symptom in ulcer located in Meckel's diverticulum. Only in a few cases (see table) is this clinical observation missing, but then the presence of an anæmia can now and then be detected. In only one of the recorded cases has hæmatemesis occurred, which is a natural consequence of the position of the lesion far down in the alimentary tract. This position, rather far away from the main source of gastric juice, also explains why the discharge of bright, red blood could be observed in certain cases.

Perforation of ulcer in Meckel's diverticulum occurs in about half of the cases, is usually preceded by pains and repeated hæmorrhages but on occasion there is no noteworthy warning. The situation is far more dangerous than in cases of perforated gastric or duodenal ulcers, because the contents of the ileum are more infective. The regular consequence is a diffuse purulent peritonitis, more rarely walling off and resulting in local peritonitis.

The diagnosis of an ulcer in Meckel's diverticulum affords great difficulties, but with the increased knowledge of this ulcer location, is not impossible. This is shown among other things by the fact that some of the authors (Stulz-Woringer, A. Jackson, Aschner-Karelitz), who observed more than one case, were subsequently able to make a correct pre-operative diagnosis.

The *differential diagnoses*, which may be considered as more directly coming into question in the age-groups concerned, are intussusception and rectal polyps. In intussusception, the hæmorrhage is, as a rule, relatively slight and mixed with mucus, which in conjunction with possible findings from palpation and X-ray examination, usually indicates the diagnosis. In low rectal polyps, the hæmorrhagic source can often be palpated or detected by proctoscopy.

In cases of Meckel's diverticulum ulcers in which perforation already has occurred, operation is, as a rule, performed on the diagnosis of acute appendicitis. In all acute surgical abdominal conditions, in which the findings at operation are not sufficient to account for the symptoms, a search should be made for a Meckel's diverticulum. Failure to do this has, in several cases, as can be gathered from the Table, led to a lethal result from continued peritonitis.

Gastro-intestinal X-ray examination has been made in some cases without positive findings, but may be helpful in excluding a gastroduodenal ulcer as the cause of bleeding.

Pathological anatomy. Meckel's diverticulum is, as is well known, an anomalous remainder of the omphalomesenteric or vitelline duct, which is found in 1 to 2 per cent of all autopsies and twice as frequently in males as in females. Various evolutionary degrees of this rest (fistula, cyst, diverticulum) can be met with, from a persistent duct between the intestine and navel, to a slight prolapse of a mucous membrane at the umbilicus.[1]

In about one-sixth of the cases of Meckel's diverticulum, the distinctive finding is dystopic mucosa, containing chief and acid cells and histologically completely analogous to the fundic mucosa of the stomach. As yet it has not been possible to discover any satisfactory explanation of this heterotopia,[2] but attention may be called to the fact that aberrant pancreatic tissue also occurs in Meckel's diverticulum. The fundic portions may form one or more islets at the apex of the diverticulum or if of large extent may entirely line this pouch.

It is this special category of Meckel's diverticulum that becomes the seat of ulcer formation. The fundamentally important and constantly recurring feature is that this lesion is situated within the area of the ordinary intestinal mucosa (area of activity) and regularly close against the boundary of the dystopic mucosa of fundic type (area of production). From this it follows that cases in which the foreign mucosa only forms one or more islets show the ulcer situated in the diverticulum and usually at its neck. When the entire pouch, however, is lined by gastric mucosa, we find the lesion in the ileum, close to the neck of Meckel's diverticulum (see Fig. 6). Even the macroscopical appearance presents great resemblance to the typical gastric and duodenal ulcers. This resemblance is confirmed by the microscopic picture. The cases reported in the literature as well as our own (in addition examination of two earlier cases: Gramén, Buechner), regularly present the character of a round ulcer with sharp, stamped-out margins, disrupted muscularis, and a callous base. The surrounding mucous membrane may show a very slight chronic irritation, with hyperæmia and cellular infiltration under an intact surface epithelium, analogous perhaps to an ulcer gastritis, but graver inflammatory changes are never seen. Thus, these cases do not present any diverticulitis resembling a gangrenous appendicitis with perforation, although it is possible for inflammatory changes of the last mentioned nature to occur in Meckel's diverticulum.

That these dystopic portions of mucous membrane in Meckel's diverticulum do not merely resemble fundic mucosa morphologically, but are also functionally active, has been amply demonstrated by analysis of their secretion in

[1] Amply discussed with illuminating figures by T. S. Cullen, The Umbilicus and Its Diseases, Philadelphia, 1916.

[2] Discussed fully by E. Goetsch, Johns Hopkins Hosp. Bull., 1919, xxx, 143-161.

cases of open umbilical fistula. Both pepsin and hydrochloric acid have been detected by Tillmanns, Lexer, Denucé, Rosthorn, Stone, A. L. Taylor. As observed by these investigators, this secretion clearly begins or increases synchronously with the activity of the stomach. This is in accordnace with Ivy's experiments on transplanted fundic mucosa in the mammæ of dogs, where the transplant was likewise found to secrete gastric juice in connection with feeding. This implies that the production of gastric juice in Meckel's diverticulum occurs at a time during which the small bowel is empty and when no neutralization takes place by food and intestinal juice. In such manner especially favorable conditions are created for the generation of peptic lesions, a circumstance that we find borne out by the occurrence of these ulcers in Meckel's diverticulum even at an early age. This early age incidence affords the only obvious point of difference between the Meckel's diverticulum lesions and the ordinary gastric and duodenal ulcer.

A summary of the facts elicited from the study of ulcers in Meckel's diverticulum brings out the following points against Konjetzny's previously cited view: a production of gastric juice from dystopic mucosa is proved by the cases of umbilical fistula. This secretion comes into contact with the small intestine when the latter is empty and therefore without any acid-neutralizing agent. Both macroscopically and microscopically the lesions present the typical picture of a round ulcer, and like this are always located within the area of activity of the hydrochloric acid. Lastly, the clinical symptoms presented by ulcer in Meckel's diverticulum, i.e., pains, hæmorrhages, and perforation, show striking analogy to those in the classical gastric and duodenal ulcer. It may, therefore, be considered as justifiable also to class the peptic lesions which are encountered in Meckel's diverticulum with the ulcer disease.

POSTOPERATIVE JEJUNAL ULCER

Ulcers of the type dealt with in this article are under ordinary conditions not met with in the jejunum. This is attributed to the fact that the acid gastric juice is neutralized by the bile and pancreatic juice, with the result that peptic ulcers do not occur below Vater's ampulla. An instructive instance of this is Holzweisser's case, cited by Hauser. In this patient, a woman of 58 years with an obstructed ampulla, eight characteristic erosions and ulcers had developed below the duodenojejunal flexure.

The state of things is quite different if through surgical measures (gastro-enterostomy, Billroth II) the jejunal mucosa has been brought in juxtaposition with the gastric, for then jejunal ulcers may arise as a not particularly uncommon complication. In about half of the cases the lesions are situated at the anastomosis (gastrojejunal ulcer), the rest lie farther down the jejunum, and as a rule in the efferent loop (jejunal ulcer). Histologically they are of the same type as gastric and duodenal ulcers.

Opinions differ as to the mode of origin of these jejunal ulcers. Many authors, especially surgeons, have emphasized mechanical disturbances produced by the operations, with interference with the blood supply or irritation from suture material. This does not, however, explain the jejunal ulcers present below the point of anastomosis, and there still remains unexplained the fact that postoperative jejunal ulcers occur extremely rarely in cases of gastro-enterostomy for cancer of the stomach (with reduced or absent hydrochloric acid).

Closer patho-anatomical inquiry has revealed, however, that postoperative jejunal ulcer arises like other peptic ulcers, associated with an inflammatory change in the intestinal mucosa. Even a gross examination is able to show considerable thickening of the wall as well as hyperæmia in the efferent loop, and at times in the adjacent portion of the afferent loop. On microscopic examination, also confirmed by two of our own cases, we encounter the picture of a jejunitis (Heidbreder, Chiari, Winkelbauer-Hogenauer) analogous to the corresponding gastric and duodenal changes.

This jejunitis is characterized by great dilatation of vessels, considerable infiltration of cells with eosinophilic leucocytes and plasmacells, as well as an increase of connective tissue in the submucosa.

Both Konjetzny and Puhl have described severe jejunitis with scattered erosions in the loop of the gastro-enterostomy. Of further interest is the fact that at von Bergmann's clinic it has been possible to establish radiologically the presence of jejunal mucous membrane changes in 100 per cent of the cases of postoperative jejunal ulcer.

In the case of jejunitis, too, the Kieler school denies that the gastric juice is the primary factor in the generation of these inflammatory changes and condemns the designation "peptic jejunal ulcer." However, the majority of authors hold to the dominating influence of the gastric juice. A peptic jejunal ulcer is accordingly seen to originate only when hydrochloric acid is left in the stomach after an operation, and consequently much oftener after a simple gastro-enterostomy than after a resection. We thus meet, in analogy to the cases of ulcer in Meckel's diverticulum, intestinal mucous membrane directly exposed to the action of hydrochloric acid. This action, evidenced by the jejunitis, ceases in that portion of the bowel where there is an opportunity for the duodenal juice to neutralize the peptic factor (e.g., at the point of a Braun's anastomosis).

Peptic jejunal ulcer occurs more frequently in males and most often in the young. Perhaps there exist in these cases factors that are more tangibly constitutional, expressing themselves, for instance, in the recurrence again and again of a peptic ulcer despite repeated operations. A particularly instructive case in this respect is that described by G. Petrén. This patient underwent 6 laparotomies, 3 of which were for perforation.

CONCLUSIONS

A survey of the experiences acquired will show that, in the biochemical theory, we have an exceedingly good explanation of the nature as well as the location of the peptic lesions with ulcer formation, confined to the œsophagus, cardia, area of pyloric glands, duodenum, jejunum (postoperatively), and in Meckel's diverticulum. Everywhere the lesion is to be found in the area of activity of the hydrochloric acid. The presence of free hydrochloric acid has likewise proved to be a regular finding and furthermore certain factors that render an excess of the acid possible have been discussed. Buechner's widely laid experiments constitute a powerful support for the trend of opinion he represents.

Our analysis of published cases and of our own cases of ulcer in Meckel's diverticulum has, as against Konjetzny's view, shown the profound clinical and patho-anatomical accordance of this lesion with the typical gastric and duodenal ulcer.

In Buechner's account, the detailed histological description of the most acute changes of fibrinoid necrosis occupies a large space. To this one may perhaps object that even if the presence of this fibrinoid necrosis accords very well with the assumption of an acid effect, it would nevertheless be safest to draw no extreme conclusions regarding the etiology of this necrosis on the strength of the histological picture. As a matter of fact, the establishment of the position of the lesions and of the occurrence of ulcer in Meckel's diverticulum provides stronger proof of the peptic factor.

This biochemical theory, now advanced anew and further developed by Buechner, has, in fact, been taken up and confirmed by several leading investigators.

Aschoff, who was able to follow Buechner's researches most intimately, associated himself with the peptic point of view in his Nothnagel lecture (published in 1929). In like manner, another pioneer in this field of research, namely Moszkowicz, 1930, declared himself to share the same opinion. Great interest attaches to the fact that in his excellent monograph on "Magen-und Duodenalgeschwuer," Kalk, from von Bergmann's clinic, expresses the opinion that the gastric juice has again marched to the foreground as a genetic factor of ulcer, contending however, that the excess of hydrochloric acid is due to a "Dysharmonie des vegetativen Nervensystems." Lastly, Buechner's view has recently been endorsed also from a surgical source (von Haberer).

With reference to the therapeutic bearing of the view of ulcer genesis maintained in the foregoing, the following may be quite generally said. The main object would be to

control and reduce as far as possible the production of hydrochloric acid by suitable dieting in accordance with the experiences gained chiefly through the Pavlov school, these experiences having already been applied at many clinics. It will, however, be necessary to devote greater attention than before to the psychic phase of acid secretion in a fasting stomach. The old clinical observation of the beneficent and healing effect of alkaline treatment, more closely worked out by Sippy, also receives further support by putting the action of the acid gastric juice in the foreground.

Considering surgical therapy with its rather varying measures, the operation, Billroth I, which reduces the production of hydrochloric acid, removes that part of the gastral system which is most susceptible to ulceration while retaining to the greatest possible extent the normal topography and normal discharging conditions, is probably the method that yields the best results and shows extremely few or no cases of relapse or postoperative ulcer (von Haberer, Bohmansson).

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THE NATURE OF THE AMNIOTIC FLUID

A Comparative Study of Human Amniotic Fluid and Maternal Serum[1]

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THE source and nature of the amniotic fluid, its rate of formation, the mode of reabsorption, if reabsorption occurs, the factors which govern its volume, are all matters of conjecture concerning which but little data exist. Even the chemical composition has been studied in detail by only one modern investigator. This interesting and important fluid is not mentioned in most textbooks of physiology and biochemistry.

In this paper we are reporting comparative studies upon the human amniotic fluid and maternal blood in 33 instances, and studies upon the amniotic fluid alone in 3 instances.

Our data lend support to the theory that the amniotic fluid is primarily a dialysate of either maternal or fetal blood, diluted to a varying extent by fetal urine.

METHODS

The amniotic fluid was obtained in two ways. One method was to use a large bore needle, puncture the unruptured bag of forewaters as it presented at the vulva, and draw the fluid into a syringe; the other was to expose the unruptured membranes at cæsarean section and withdraw the fluid with syringe and needle. Occasionally, the amniotic fluid was contaminated with a slight amount of blood. All fluids, except those obtained early in pregnancy, which were clear, were centrifuged to remove the vernix casiosa.

Blood was obtained from an arm vein without stasis and received directly under oil. The blood was centrifuged under oil and the serum pipetted off, placed under oil, and kept cool until used. In all except 3 cases the amniotic fluid was obtained before the sample of blood. These time relationships and types of anæsthesia and operation are shown in Table V.

Total solids were determined gravimetrically upon 1 or 2 cubic centimeter samples dried to a constant weight between 105 degrees and 110 degrees C. Specific gravity was done by the drop method of Barbour and Hamilton. The depression of the freezing point was determined with the Beckmann cryoscopic apparatus, a Heidenhain thermometer and a mechanical stirring device being used (Findlay). Chlorides were determined either by the method of Van Slyke or by the modification of Wilson and Ball. We obtained identical results by these two methods before adopting the modification. Sodium determinations were done by the Rourke modification of the Kramer and Gittleman method. Calcium was determined by an unpublished method of Fiske. The total nitrogen of the serum was obtained by the Dyer modification of the Kjeldahl method 1 cubic centimeter of serum being used. The total protein of the serum was calculated by subtracting the non-protein nitrogen from the total nitrogen and multiplying by 6.25. The total protein in the amniotic fluid was determined by the method of Denis and Ayer, and in 4 instances checked by the macro-Kjeldahl method (Table I). The agreement was very satisfactory. Non-protein nitrogen and creatinine were determined by the method of Folin and Wu. The total reducing substances were determined by the Folin and Wu method using the modified sugar tubes of Rothberg and Evans.

Yeast fermentation was determined by the method described by Benedict. Hydrolysis was done according to the method used by Folin and Berglund.

Osazones of the sugars were formed using a phenyl-hydrazine-sodium acetate mixture as described by Hawke and Bergeim in their textbook. The protein was removed from the amniotic fluid, before the phenyl-hydrazine mixture was added, by adding a few drops of a 5 per cent solution of acetic acid, heating on a water bath for 2 to 3 minutes, and then shaking with purified animal charcoal and filtering. Six or 7 cubic centimeters of this filtrate were used for the osazone reaction.

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TABLE I.—COMPARISON OF AMNIOTIC FLUID PROTEIN VALUES DETERMINED BY MACRO-KJELDAHL AND BY DENIS-AYER METHODS

	Milligrams per 100 cubic centimeters			
	Case 1	Case 25	Case 29	Case 33
Total nitrogen by Kjeldahl	92	171	107	67
Non-protein nitrogen	29	21	25	35
Protein by Kjeldahl (protein N x 6.25)	394	938	512	200
Protein (Denis-Ayer)	354	999	570	160

TABLE II.—AVERAGE FIGURES (SEVEN CASES) OF ZANGEMEISTER AND MEISSL[1] FOR MATERNAL SERUM, FETAL SERUM, AND AMNIOTIC FLUID

	Maternal serum	Fetal serum	Amniotic fluid
Freezing point,—.° C.	.537	.537	.482
Specific gravity	1.0264	1.0219	1.0074
Chloride (as NaCl), mgms. per c.cm.	627	625	620
Total nitrogen, mgms. per c.cm.	1104	844	54
Rest nitrogen, mgms. per c.cm.	22	19	23
Protein, mgms. per c.cm.	6790	5160	220

LITERATURE

Williams, 1930, states that there are four main views as to the origin of the amniotic fluid: (1) fetal urine, (2) transudation from maternal blood, (3) secretion through amniotic epithelium, (4) mixed origin. Portal, according to Williams, in the 17th century, suggested that the amniotic fluid consisted of fetal urine.

Schmidt, on the basis of histological studies, believed that the amniotic fluid is secreted by the placental amniotic epithelium (the cells of the amnion near the center of the placenta are high columnar gradually becoming cuboidal toward the periphery, and almost flat opposite the placenta).

Wagner believed that the fetal kidneys of animals function only when the maternal kidneys have been largely destroyed.

Reinwein and Heinlein, on the other hand, found in the amniotic fluid of the cow, benzoic acid, hippuric acid, creatinine, histidine and methyl guanidin, and conclude that amniotic fluid is a waste product similar to urine.

Uyeno made a careful study of the physical and chemical properties of human amniotic fluid. This is the most important study of this sort in the literature. Uyeno gives no data on maternal blood, however, nor does he draw conclusions from his data as to the nature of the amniotic fluid. In general his data closely resemble our own. The few significant differences will be discussed below.

One of the earliest and by far the most important comparative studies of amniotic fluid and maternal and fetal blood is that of Zangemeister and Meissl in 1903. These investigators determined the freezing point, specific gravity, chloride, nitrogen, rest-nitrogen, and protein in nearly simultaneous samples of human maternal blood, fetal blood, and amniotic fluid in 7 cases at term, one of which consisted of identical twins. In this case both the amniotic fluids were examined. The averages of their figures are presented in Table II. The maternal and fetal sera were isotonic within 0.005 degrees in all but 1 case in which a freezing point difference of 0.015 degrees was found. The chloride content of these two sera was also nearly identical, the greatest difference being 15 milligrams per 100 cubic centimeters. The specific gravity of the fetal serum was uniformly less than that of the maternal serum as were also the total nitrogen and protein contents. The rest-nitrogen was also less in the fetal serum in all but one case in which the rest-nitrogen was identical in the two fluids. These findings justify the conclusion that at term fetal blood is in osmotic equilibrium with maternal blood and essentially identical in composition with it except for the lower plasma protein content. The lower protein content of the fetal blood has been subsequently confirmed by Plass and Matthew.

Zangemeister and Meissl found the amniotic fluid to be always hypotonic to maternal and fetal sera, the amniotic fluid freezing at from .033 to .080 degrees C. higher than the maternal serum. The chloride content of the amniotic fluid closely paralleled that of the two sera but averaged slightly less. The specific gravity, total nitrogen and protein content were much less than that of the sera in all cases. The rest-nitrogen of the amniotic fluid was usually greater than that of the maternal and fetal sera. It will be seen later that these findings closely resemble our own.

Zangemeister and Meissl showed that the hypotonicity of the amniotic fluid could not be due to excess of carbon dioxide in the sera; for they were unable to lower the osmotic

[1]Muenchen. med. Wchnschr., 1903, 1:673.

pressure appreciably by aerating the blood serum with hydrogen. They reasoned that the lower osmotic pressure of the amniotic fluid could be explained only by a dilution with some hypotonic solution. They then presented data on the freezing point of 9 samples of urine of newborn infants—these ranged from −0.148 degrees to −0.340 degrees C. with an average value of −0.203 degrees C. The chloride (sodium chloride) contents of these urines ranged from 123 to 403 milligrams per 100 cubic centimeters with an average value of 299 milligrams per 100 cubic centimeters. These urines were all protein free. The urines of four infants 24 hours to 6 days old had freezing points ranging from −0.609 degrees to 1.064 degrees C., while the chloride was only moderately increased ranging from 227 to 441 milligrams per 100 cubic centimeters. The increased concentration of urine in the first few days after birth is therefore due chiefly to substances other than chlorides. These are present only in small amounts in fetal urine.

Zangemeister and Meissl calculated that 16.5 per cent of amniotic fluid must be fetal urine to give the amniotic fluid its average concentration. This would mean an average of 81 cubic centimeters of urine (amniotic fluid volume taken as 500 cubic centimeters). As, however, there must constantly be a tendency for the amniotic fluid to be approaching an equilibrium with the maternal or fetal blood, somewhat more than this amount of urine would be required. As the fetus could not form 81 cubic centimeters of urine during labor, fetal urine must be forming in the latter portion of pregnancy, particularly as in a few instances amniotic fluid obtained before or just at the onset of labor was definitely hypotonic to maternal blood. In one case of abortion at 5 months (fetal length 25 centimeters) the maternal serum had a freezing point of −0.535 degrees C. and the amniotic fluid 0.520 degrees C. (This amniotic fluid was coffee-brown and contained 0.69 per cent methæmoglobin.) Zangemeister and Meissl concluded that as early as the fifth month of pregnancy the amniotic fluid must be diluted with an appreciable amount of fetal urine.

These data of Zangemeister and Meissl have been given in some detail because it is the most important in the literature and because our own data are closely parallel.

Gruenbaum agrees with Zangemeister and Meissl that the amniotic fluid is hypotonic to maternal serum and quotes several authors to this effect. He emphasizes the fact that Jacque found at 6 months' pregnancy the freezing point of the amniotic fluid −0.520 degrees C. and that of the fetal blood −0.530 degrees C. Gruenbaum presents data on the amniotic fluid in one case at 8 weeks of pregnancy. Nine cubic centimeters of clear fluid were obtained, slightly alkaline to litmus, with a dry weight of 1.048 per cent, ash 0.606 per cent, and freezing point −0.495 degrees C. Unfortunately, the maternal blood was not examined. Gruenbaum concludes that in the earlier months of pregnancy there is less difference in freezing point depression between amniotic fluid and maternal blood than at term.

RESULTS

Our data on maternal serum and amniotic fluid in 21 cases at term are shown in Table III and in 15 cases earlier in pregnancy are shown in Table IV.

In general our findings are similar to those reported by Zangemeister and Meissl and by Uyeno. Our values for chloride in the amniotic fluid, however, are somewhat higher than those reported by these observers. The values of Williams and Bargen for chlorides in amniotic fluid are so low, averaging 5.93 milligrams per 100 cubic centimeters in normal fluids, as to be inexplicable except on the basis of a misprint. As is shown in Table II, Zangemeister and Meissl found the chloride value in the amniotic fluid close to, but averaging slightly less than, that in the maternal serum. In our cases at term (Table III) the average value was definitely higher in the amniotic fluid than in the maternal serum. In 7 cases only was the relation reversed, the greatest excess in the serum being 20 milligrams per 100 cubic centimeters (Case 5), while 8 cases showed an excess of chloride in the amniotic fluid of from 30 to 124 milligrams per 100 cubic centimeters. In all of the 12 cases before term (Table IV) the amniotic

TABLE III.—AMNIOTIC FLUID AND MATERNAL SERUM AT TERM

Case No.	Protein		N.P.N. mgms./100c.cm.		Sugar mgms./100c.cm.		Chloride mgms./NaCl-100 c.cm.		Sodium mgms./100c.cm.		Calcium mgms./100c.cm.		Creatinine mgms./100c.cm.		Specific gravity		Total Solids mgms./100 gms.		Freezing-point—°C.		Months of pregnancy
	Serum gms./00 c.cm.	Am.Fl. mgms/.00 c.cm.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl	Serum	Am.Fl.	
1	5.8	354	29	29	105	25	644	665							1.0273	1.0078	9.01	1.23	.526	.502	Nine
2	6.6	165	25	22	73	11	591	594							1.0250	1.0068	10.04	1.16	.532	.466	Nine
3	6.0	168	23	25	98	30	615	615							1.0239	1.0071	7.85	1.17	.539	.483	Nine
4	5.6	174	24	31	106	29	633	664							1.0222	1.0072	7.41	1.19	.543	.509	Nine
5	6.8	231	19	22	120	25	645	625							1.0254	1.0066	8.34	1.16	.563	.498	Nine
6	6.2	249	22	33	127	28	585	623							1.0200	1.0078	8.31	1.27	.554	.502	Nine
7	6.5	502	26	29	145	48	607	667							1.0248	1.0086	8.30	1.47	.561	.536	Nine
8	6.8	105	20	26	114	31	567	559							1.0248	1.0062	9.37	1.01	.567	.463	Nine
9	6.6	228	23	37	150	30	593	578							1.0257		8.50		.558	.502	Nine
10	5.3	174	22	26	93	40	627	616							1.0215	1.0068	7.80	1.09	.538	.466	Nine
11	6.0	138	25	25	153	28	593	641							1.0225	1.0074	8.20	1.20	.533	.497	Nine
11*		19			55		720														Nine
12		276	32	20	145	47	596	596							1.0228	1.0077	8.14	1.42			Nine
13	5.7	264	21	28	116	29	604	634							1.0226	1.0078	8.31	1.11	.562	.516	Nine
13*		26			62		740														
14	6.5				114	20	601	582	341	294									.552	.488	Nine
15	6.4	219	25	21	101	30	623	658	285	283	8.8	5.3					8.20	1.13	.552	.504	Nine
16	6.3	219	25	24	104	58	627	667	321	314	8.0	7.3							.543	.521	Nine
17	5.4	250	21	27	78	25	619	614	308	288							7.29	1.13	.570	.515	Nine
18	5.5	150	21	39	132	26	619	632	290	273			1.67	2.30					.573	.513	Nine
19	6.5		21	18	118	62	481	605	322	301			1.54	2.61				1.29	.541	.500	Nine
20							601	588	310	283			1.43	2.00				1.18		.509	Nine
21	6.1	324	31	27	79	32	616	634							1.0239	1.0077	8.87	1.34	.561	.540	Nine
High	6.8	502	32	39	153	62	645	667	341	314					1.0273	1.0086	10.04	1.47	.573	.540	
Low	5.3	105	19	18	73	11	481	559	285	273					1.0200	1.0062	7.29	1.01	.526	.463	
Average	6.1	233	24	27	114	33	604	622	311	291	8.4	6.3	1.55	2.30	1.0237	1.0073	8.37	1.21	.551	.502	

*Figures in this line are for spinal fluid.

TABLE IV.—AMNIOTIC FLUID AND MATERNAL SERUM BEFORE TERM

Case No.	Protein		N.P.N. mgms./100c.cm.		Sugar mgms./100c.cm.		Chloride mgms./NaCl-100 c.cm.		Sodium mgms./100c.cm.		Calcium mgms./100c.cm.		Creatinine mgms./100c.cm.		Specific gravity		Total Solids mgms./100 gms.		Freezing-point—°C.		Months of pregnancy
	Serum gms./00 c.cm.	Am.Fl. mgms/.00 c.cm.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am. Fl	Serum	Am.Fl.	
1	5.8	354	29	29	105	25	644	665							1.0273	1.0078	9.01	1.23	.526	.502	Nine
2	6.6	165	25	22	73	11	591	594							1.0250	1.0068	10.04	1.16	.532	.466	Nine
3	6.0	168	23	25	98	30	615	615							1.0239	1.0071	7.85	1.17	.539	.483	Nine
4	5.6	174	24	31	106	29	633	664							1.0222	1.0072	7.41	1.19	.543	.509	Nine
5	6.8	231	19	22	120	25	645	625							1.0254	1.0066	8.34	1.16	.563	.498	Nine
6	6.2	249	22	33	127	28	585	623							1.0200	1.0078	8.31	1.27	.554	.502	Nine
7	6.5	502	26	29	145	48	607	667							1.0248	1.0086	8.30	1.47	.561	.536	Nine
8	6.8	105	20	26	114	31	567	559							1.0248	1.0062	9.37	1.01	.567	.463	Nine
9	6.6	228	23	37	150	30	593	578							1.0257		8.50		.558	.502	Nine
10	5.3	174	22	26	93	40	627	616							1.0215	1.0068	7.80	1.09	.538	.466	Nine
11	6.0	138	25	25	153	28	593	641							1.0225	1.0074	8.20	1.20	.533	.497	Nine
11*		19			55		720														Nine
12		276	32	20	145	47	596	596							1.0228	1.0077	8.14	1.42			Nine
13	5.7	264	21	28	116	29	604	634							1.0226	1.0078	8.31	1.11	.562	.516	Nine
13*		26			62		740														
14	6.5				114	20	601	582	341	294									.552	.488	Nine
15	6.4	219	25	21	101	30	623	658	285	283	8.8	5.3					8.20	1.13	.552	.504	Nine
16	6.3	219	25	24	104	58	627	667	321	314	8.0	7.3							.543	.521	Nine
17	5.4	250	21	27	78	25	619	614	308	288							7.29	1.13	.570	.515	Nine
18	5.5	150	21	39	132	26	619	632	290	273			1.67	2.30					.573	.513	Nine
19	6.5		21	18	118	62	481	605	322	301			1.54	2.61				1.29	.541	.500	Nine
20							601	588	310	283			1.43	2.00				1.18		.509	Nine
21	6.1	324	31	27	79	32	616	634							1.0239	1.0077	8.87	1.34	.561	.540	Nine
High	6.8	502	32	39	153	62	645	667	341	314					1.0273	1.0086	10.04	1.47	.573	.540	
Low	5.3	105	19	18	73	11	481	559	285	273					1.0200	1.0062	7.29	1.01	.526	.463	
Average	6.1	233	24	27	114	33	604	622	311	291	8.4	6.3	1.55	2.30	1.0237	1.0073	8.37	1.21	.551	.502	

*Figures in this line are for spinal fluid.

TABLE IV.—AMNIOTIC FLUID AND MATERNAL SERUM BEFORE TERM

Case No.	Protein		N.P.N. mgms./100c.cm.		Sugar mgms./100c.cm.		Chloride mgms./NaCl-100 c.cm.		Sodium mgms./100c.cm.		Calcium mgms./100c.cm.		Creatinine mgms./100 c.cm.		Specific gravity		Total solids gms./100 gms.		Freezing-point—.°C.		Months of pregnancy
	Serum gms./100 c.cm.	Am.Fl. mgms./100 c.cm.	Serum	Am.Fl.	Serum	Am.Fl.	Serum	Am.Fl.	Serum	Am.Fl.	Serum	Am.Fl.	Serum	Am. Fl.	Serum	Am. Fl.	Serum	Am.Fl.	Serum	Am.Fl.	
22	5.2	231	31	36	125	22	599	639							1.0210	1.0076	7.00	1.29	.554	.506	Eight
23	5.5	1050	24	21		23	592	645	313	309				1.60						.520	Eight
24	5.7	506	24	18	138	11	612	633													Seven-Eight
25	6.1	999	29	21	88	16	638	686							1.0237	1.0121	7.72	1.81	.550	.526	Seven
26	5.9	492	34	26	93	21	593	725							1.0234	1.0087	7.07	1.51	.557	.541	Six
27	5.7		23	27	125	44	610	641	313	296	8.6	5.6					8.96	1.52	.562	.527	Six
28	6.3	133	24	22	127	64	604	641							1.0250	1.0089	8.29	1.21	.557	.537	Five
29	6.2	570	24	25		42	614	649	306	303			1.39	1.43			8.33	1.62	.539	.532	Four
36		308					601	641											.567	.552	Four
30	6.2	342	17	25	108	44	610	641	300	301	9.6	8.8					8.67	1.07	.589	.539	Three-Four
31	6.7	120	18	25	142	86	584	615	311	300	8.5	7.4							.547	.562	Three-Four
31*		†					711		316									†			
32		100		25		72		642				8.7				1.0082				.521	Three
33		160		35		52		655								1.0086		1.36		.542	Three
34		126		34		51		670								1.0077					Two-Three
35	6.6	166	23	18			588	605							1.0262	1.0078	7.96	1.10	.553	.556	Two-Three
High	6.7	1050	34	36	142	86	638	725	313	309					1.0262	1.0121	8.96	1.81	.589	.562	
Low	5.2	100	17	18	88	11	584	605	300	296					1.0210	1.0076	7.00	1.07	.539	.506	
Average	6.0	378	25	26	118	42	604	648	309	302	8.9	7.3	1.39	1.51	1.0239	1.0087	8.00	1.39	.557	.539	

*Figures in this line are for spinal fluid.
†Spinal fluid protein normal to Pandy test.

TABLE V.—TIME RELATIONSHIPS AND TYPE OF ANÆSTHESIA

Case No.	Interval between time of obtaining amniotic fluid and blood	Anæsthetic	Comment
1	15 mins.	None	5 hours' labor
2	15 mins.	None	12 hours' labor
3	30 mins.	Gas-oxygen and ether	
4	30 mins.	Gas-oxygen for 10 minutes	
5	25 mins.	Gas-oxygen and ether	
6	60 mins.	Gas-oxygen and ether	
7	20 mins.	Gas-oxygen and ether	
8	30 mins.	Gas-oxygen and ether	
9	30 mins.	Gas-oxygen and ether	
10	45 mins.	Spinal, morphine, scopolomine, and gas-oxygen	Cæsarean section
11	30 mins.	Spinal, morphine and scopolomine	Cæsarean section
12	30 mins.	Gas-oxygen and ether	Cæsarean section
13	60 mins.	Spinal, morphine and scopolomine	Cæsarean section
14	45 mins.	Spinal	Cæsarean section
15	40 mins.	Spinal	Cæsarean section
16	40 mins.	Spinal	Cæsarean section
17	30 mins.	Gas-oxygen and ether	Cæsarean section
18	45 mins.	Gas-oxygen and ether	Cæsarean section
19	30 mins.	Gas-oxygen and ether	Cæsarean section
20	Blood taken before operation	Gas-oxygen and ether	Cæsarean section
21	30 mins.	Spinal, morphine and scopolomine	Cæsarean section
22	45 mins.	Gas-oxygen and ether	Cæsarean section
23	Blood taken before anæsthetic	Gas-oxygen and ether	Hydramnios, ruptured membranes and anencephaly
24	15 hrs.	None	Hydramnios, ruptured membranes
25	10 mins.	Gas-oxygen	Cæsarean section
26	45 mins.	Local, morphine and scopolomine	Cæsarean section
27	30 mins.	Local, gas-oxygen and ether, morphine and scopolomine	Cæsarean section
28	45 mins.	Spinal, morphine and scopolomine	Hysterectomy
29	30 mins.	Spinal	Hysterectomy
30	40 mins.	Spinal, gas-oxygen	Hysterectomy
31		Spinal, gas-oxygen	Hysterectomy
32			Hysterectomy
33		Morphine, scopolomine, gas-oxygen, and ether	Hysterectomy
34		Spinal, morphine and scopolomine	Hysterectomy
35	Blood taken before anæsthetic	Gas-oxygen and ether	
36	Blood taken before anæsthetic		Hysterectomy

fluid chloride was definitely higher than that in the maternal serum. In the few cases in which calcium was determined, our values are definitely lower than those reported by Uyeno. Uyeno was not able to demonstrate the presence of creatinine or sugars in the amniotic fluid. Williams and Bargen, however, found creatinine and reducing substances in the amniotic fluid. Here, as in the case of chlorides, their figures are so bizarre that some error in the position of the decimal point must be assumed. It is, therefore, futile to compare their figures with ours. In 7 instances we have determined creatinine in maternal blood and amniotic fluid, and in every instance the amount in the amniotic fluid exceeded that in the serum (Tables III and IV). As the color produced in the Folin and Wu method is not specific for creatinine, and as we have not identified creatinine as such in the amniotic fluid, there is no assurance that creatinine was actually present in the amounts indicated. The reducing substances in the amniotic fluid, determined by the method of Folin and Wu and calculated as glucose, ranged from 11 to 62 with an average of 33 milligrams per 100 cubic centimeters, in the cases at term (Table III), while in the cases before term the range was from 11 to 86 with an average of 42 milligrams per 100 cubic centimeters (Table IV). The maternal serum sugar in these two groups of cases averaged 114 to 118 milligrams per 100 cubic centimeters, respectively.

The characteristic osazones of glucose and of lactose were formed in the protein free filtrate of several but not all fluids at term, while in one case at from 3 to 4 months' pregnancy, the osazone of glucose but not that of lactose was demonstrated. We have also demonstrated the presence of a fermentable reducing substance, presumably glucose, in 13 samples of amniotic fluid. The total reducing substances were significantly lowered by yeast fermentation in every case. In 1 case the reducing substances dropped from 58 to 4 milligrams per 100 cubic centimeters after fermentation with yeast. In 8 of these instances mild hydrochloric acid hydrolysis of the protein free filtrate after yeast fermentation produced an increase in the reducing substances in 4 cases at term suggesting the presence of di -or polysaccharides, while 3 cases early in pregnancy and 1 at term showed no such increase in reducing substances after hydrolysis. These data are shown in Table VI. They indicate the presence of small amounts of glucose in human amniotic fluid and sug-

gest that di- or polysaccharides (lactose) may be present in small quantities at term.

In agreement with Zangemeister and Meissl, we have found the amniotic fluid to be hypotonic to the maternal serum at term. We were unaware of this earlier work of Zangemeister and Meissl until after our data had been collected. It is interesting, therefore, that we should have followed the same reasoning and reached the same conclusions in trying to explain the hypotonicity of the amniotic fluid.

DEDUCTIONS

During the past eight years two of us (F.F.S and M.E.D.) have been making comparative studies between human blood serum and various body fluids, particularly the cerebrospinal fluid. This fluid, which is a nearly protein free dialysate, isotonic with the blood plasma and in osmotic equilibrium with it, has, however, a much higher chloride content than the blood serum or plasma and this difference in chloride is believed to compensate for the almost complete absence of proteins or other colloids from the cerebrospinal fluid (Mestrezat). We have found in various body fluids (pleural, peritoneal, and œdema fluids) that the higher the protein content of the fluid, i.e., the nearer its protein content approaches that of the blood serum, the less excess of chloride will the fluid contain (10).

Our idea in examining the amniotic fluid was to compare it with cerebrospinal fluid, expecting that it would also be a relatively protein free dialysate in equilibrium with either maternal or fetal serum. When we found that the amniotic fluid was regularly hypotonic to the serum we reasoned that if the amniotic fluid was originally a dialysate in equilibrium with the blood, it must be diluted appreciably at term with some distinctly hypotonic fluid. We were able to obtain three samples of fetal urine, two at term and one at 6 months. These are presented in Table VII. The data are very similar to that obtained by Zangemeister and Meissl previously mentioned. Urine is present in the bladder earlier than this for in one case at 3 to 4 months' pregnancy a few drops of urine were obtained by gentle pressure on the abdomen of the fetus. It will be seen that these urines are very dilute and, if poured into an amniotic fluid originally isotonic with blood, would render the amniotic fluid hypotonic. Now if this hypothesis be true that the amniotic fluid is originally a dialysate in equilibrium with maternal or fetal serum, later diluted by fetal urine, the earlier in pregnancy the amniotic fluid is obtained, the less fetal urine it

TABLE VI.—REDUCING SUBSTANCES

Case No.	Month of pregnancy	Total reducing substances as glucose	Residual reducing substances as glucose after yeast fermentation	Reducing substances as glucose after HCL hydrolysis of protein-free filtrate after yeast fermentation
	mgms.–100 c.cm.	mgms.–100 c.cm.	mgms.–100 c.cm.	mgms.–100 c.cm.
10	9	40	11	
11	9	28	10	
14	9	20	13	
15	9	30	9	5
16	9	58	4	15
17	9	25	12	25
18	9	26	19	29
19	9	62	30	63
21	9	32	22	
27	6	44	10	11
28	5	64	13	
29	4	41	9	9
30	3–4	44	9	9
31	3–4	86	10	

TABLE VII.—COMPOSITION OF FETAL URINE

	Case 17	Case 20	Case 27
Total nitrogen, mgms. per 100 c.cm.	43	41	61
Sugar, mgms. per 100 c.cm.	13		
Creatinine, mgms. per 100 c.cm.			4.6
Chloride (as NaCl), mgms. per 100 c.cm.	136	263	171
Freezing point, —.° C.	.141		.174
Sodium, mgms. per 100 c.cm.	6.3	26.0	14.0
Amount, c.cm.	30	5.5	25

TABLE VIII.—AVERAGE VALUES FOR NORMAL SERUM, SERUM AT TERM, CEREBROSPINAL FLUID AND AMNIOTIC FLUID

	Normal serum	Serum at term	Cerebrospinal fluid	Amniotic fluid at term	Amniotic fluid at 3–4 mos. pregnancy
Freezing-point, —.° C	.571	.551	.570	.502	.542
NaCl, mgms.–100 c.cm.	592	604	726	622	640
Sodium, mgms.–100 c.cm.	317	311	326	291	302
Calcium, mgms.–100 c.cm.	9.5	8.4	4.7	6.3	8.3
Protein, mgms.–100 c.cm.	7200	6100	29	233	226
Total Solids, gms.–100 gms.	8.96	8.37	1.10	1.21	1.26
Water, gms.–100 gms.	91.04	91.68	98.90	98.79	98.74
Sugar, mgms.–100 c.cm.	98	114	65	33	58
N.P.N., mgms.–100 c.cm.	27	24	18	27	27
Creatinine, mgms.–100 c.cm.	1.35	1.55	1.17	2.30	1.43

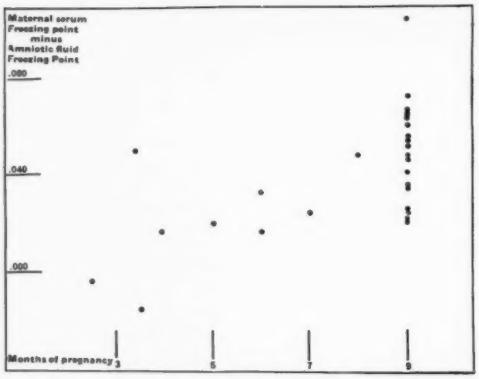

Fig. 1. This figure shows the tendency for the amniotic fluid to become more and more hypotonic to the maternal serum as pregnancy advances.

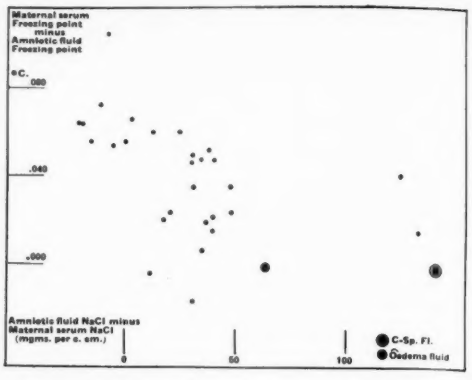

Fig. 2. This figure shows the tendency for the chloride excess in the amniotic fluid over that in the maternal serum to increase as the freezing point difference decreases, i.e., when the amniotic fluid is most nearly isotonic with maternal serum, the chloride difference between the amniotic fluid and maternal serum is greatest approaching that found between protein poor œdema fluid, or cerebrospinal fluid and the blood serum.

The average chloride difference between œdema fluids (the average of 10 cases containing less than 1 per cent protein) and blood serum as well as the average difference between normal cerebrospinal fluid and blood serum is indicated on the chart.

should contain and the more nearly isotonic with the blood it should be. Gruenbaum had already suggested that in the earlier months of pregnancy there was less difference between the freezing points of amniotic fluid and maternal serum than at term. Our data would seem to bear this out. A comparison of the freezing points in Tables III and IV shows that the average freezing point difference at term between maternal serum and amniotic fluid was .050 degrees C., while the average for the earlier months of pregnancy was only .020 degrees C. (The only instance in which the amniotic fluid was slightly hypertonic to the maternal serum occurred in this group, Case 31.) This is even more strikingly brought out in Figure 1 which shows a definite tendency for the difference in freezing point between amniotic fluid and maternal blood serum, i.e., the hypotonicity of the amniotic fluid, to increase as pregnancy advances. It should be noted that in two of our earliest cases, 29 and 35, the amniotic fluid and maternal serum were essentially isotonic. To make the picture complete a similar relationship should exist in regard to chlorides. It will be remembered that Zangemeister and Meissl found the average chloride content of the maternal serum to be 627 milligrams per 100 cubic centimeters, while that of the amniotic fluid at term was 620 milligrams per 100 cubic centimeters. In spite of the fact that these values were so nearly identical, the average freezing point depression was −0.537 degrees C. in the maternal serum and −0.487 degrees C. in the amniotic fluid (Table II). They were at a loss to account for this difference in osmotic pressure with chloride values so nearly identical. Our data at first sight would seem to increase this difficulty, for while our average figures for the freezing point of maternal serum and amniotic fluid at term −0.551 degrees C. and −0.502 degrees C. are analagous to theirs, our average chloride content of the amniotic fluid is actually greater than that of the maternal serum (maternal serum, 604 milligrams per 100 cubic centimeters; amniotic fluid, 622 milligrams per 100 cubic centimeters, Table III). Our previous experience with other body fluids has shown us that when a protein poor fluid is isotonic with the blood serum, it will always have a considerably higher chloride content. The cerebrospinal fluid is an outstanding example. Here an excess of 140 milligrams per 100 cubic centimeters are found in the cerebrospinal fluid over that in the blood serum even though the freezing points of these two fluids are identical. In œdema fluids, peritoneal, and

pleural fluids which have a considerably higher protein content than the cerebrospinal fluid, the excess of chlorides over the serum is less. On this basis we would expect the amniotic fluid, if isotonic with blood, to have a chloride content considerably higher than that of the blood serum, although not as high as that of cerebrospinal fluid, for the amniotic fluid is not as poor in protein as the cerebrospinal fluid. A comparison of blood serum, spinal fluid, and amniotic fluid is given in Table VIII. It will be seen that if the cerebrospinal fluid were diluted approximately 12 per cent, it would have a composition as regards chloride, sodium, and freezing point approximately that of the amniotic fluid, i.e., it would be definitely hypotonic to the serum but would still have a considerably higher chloride content.

A further dilution would, of course, further lower the amniotic fluid chloride till eventually it would become less than that of the maternal serum. At such a point the amniotic fluid should be considerably hypotonic to the maternal serum. In 7 cases at term the chloride content of the amniotic fluid was less than that of the serum. This was never true in the cases in which the fluid was obtained earlier in pregnancy. In 6 of these 7 cases at term with lower chloride in the amniotic fluid than in the maternal serum, the freezing points were determined and the differences ranged between −.055 and −.104 degrees C. with an average of −.069 degree C.; while in the 12 cases at term with higher chloride content in the amniotic fluid than in the maternal serum and hence presumably less dilution of the amniotic fluid, the freezing point differences ranged from −.021 degree C. to −.066 degree C. with an average of −.040 degree C. In the 10 cases at 8 months' pregnancy and earlier, in all of which the chloride content of the amniotic fluid was greater than that in the serum, the freezing point differences were even less, averaging .020 degree C. This relationship between freezing point and chloride differences is further illustrated in Figure 2. There is, therefore, a general correlation in the freezing point and chloride data which could be interpreted as indicating a gradually increasing dilution, as pregnancy progresses, of a fluid originally not unlike the cerebrospinal fluid in composition. The composition of the fetal urine is such that if added to the amniotic fluid in suitable amounts it would produce such dilution. There are many irregularities, however, in this correlation which are difficult to explain, particularly in Cases 29 and 35 where maternal serum and amniotic fluid are isotonic, a much greater excess of chloride in the amniotic fluid than actually occurs would be expected. Undoubtedly unknown factors complicate the picture.

SUMMARY

The amniotic fluid contains small amounts of a fermentable reducing substance which is undoubtedly glucose. It contains creatinine, or creatinine-like substances, in slightly greater concentration than the maternal serum. Its protein content varies from 105 to 502 milligrams per 100 cubic centimeters at term. It has slightly less sodium and usually slightly more chloride than maternal serum at term. In the earlier months of pregnancy, the chloride in the amniotic fluid is always greater than that of the maternal serum. At term the amniotic fluid is distinctly hypotonic to maternal serum, but in the earlier months of pregnancy this hypotonicity is less, and in the earliest months the amniotic fluid may be isotonic with maternal serum. Thus, early in pregnancy the amniotic fluid approaches the composition of other protein poor fluids which are in osmotic equilibrium with the blood plasma. This suggests that the amniotic fluid originates as a dialysate in equilibrium with the maternal and fetal body fluids. The fetal urine is definitely hypotonic and is present in the bladder as early as the fourth month in pregnancy. This indicates that as pregnancy advances the amniotic fluid becomes more and more diluted by the hypotonic fetal urine.

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PYELOSCOPY

A FURTHER CONTRIBUTION TO THE EXPERIMENTAL STUDY OF THE CONTRACTIONS OF THE KIDNEY PELVIS[1]

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IN former contributions (3, 4) the author has drawn attention to the clinical and experimental evidences of the contractions of the kidney pelvis. The calyces and pelvis of the kidney constitute a muscular collecting mechanism for the urine secreted by the kidney and brought down by the collecting tubules. The urine thus collected in the calyces is passed by contraction of the calyces (contracting in succession from above downward) through communicating channels to the body of the pelvis. During the systole of the calyx the corresponding communicating channel relaxes and then contracts again at the end of the calycal systole, thus constituting a muscular valve. When the three calyces have completed their systole, the body of the pelvis, which during this period has been relaxing to accommodate the urine passed in from the calyces, contracts with a snap-like action (hence suggesting the name "ventricle of the pelvis") and the "globule" of urine is passed in to the ureter along which it is carried by a peristaltic wave.

CLINICAL OBSERVATIONS

In making further observations on this subject several points of interest arise. Apparently in the contraction of the calyx the attachment around the bases of the pyramids constitutes more or less the fixed point and the contraction of the calyx commences at this point. This is in the region of the muscularis spiralis papillæ of Muschat (7). As regards the communicating channel, this becomes shorter as well as wider during the period of relaxation, and, conversely, during its period of contraction it becomes narrower and longer. Observing a series of kidneys both by pyeloscopy and pyelography, it appears that in general the lumen of each of the two upper communicating channels becomes quite obliterated at the moment of maximal contraction, while the communicating channel between the lower calyx and the body of the pelvis often remains more or less patent during the systole of the ventricle, any great degree of regurgitation being apparently prevented by the fact that the first part of the ventricle

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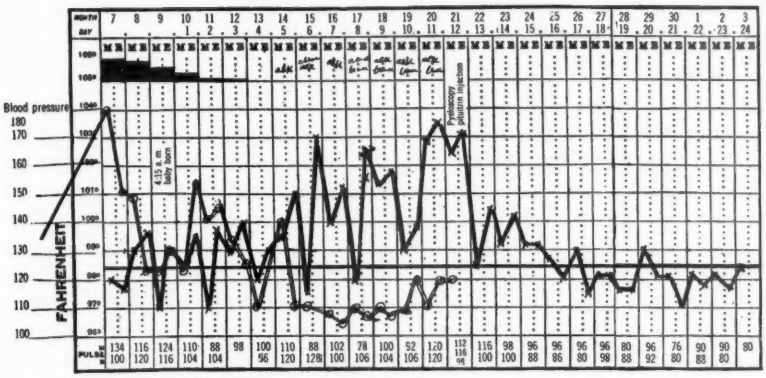


Fig. 1. Chart of Mrs. F. B. Pyelitis due to dysfunction cured by a single injection of pituitrin. Patient had had 8 convulsions before admission to hospital and one at 11:10 a.m. lasting 90 seconds, after admission. The top row of figures indicates days in hospital. The second row of figures indicates days after birth of child. The shaded areas indicate the quantities of urine. The heavy line shows temperature curve, the parallel lines the blood pressure curve.

to contract during its systole is the part in relation to the communicating channel and also the fact that the lower calyx is more or less completely contracted, being at the end of its systole, when the "ventricle" commences its systole. It was also noticed that quite commonly the uppermost communicating channel was much longer and narrower than the others, and one can easily understand how much more readily spasm could be set up in this part with consequent dysfunction, and this too was often observed in cases of pyelitis and "kidney" pain. One may concede that as a general rule dysfunction of any hollow viscus is accompanied by pain, and restoration of normal function gives relief from this pain. This condition of dysfunction no doubt accounts for many cases of obscure kidney pain in which chemical and bacteriological examination of the urine and ordinary pyelographic examination yield only obscure findings as regards causation but in which pyeloscopy will often solve the diagnosis. An interesting feature is this: quite often patients have suffered from pain or the symptoms of pyelitis off and on for weeks, months, or even years and on pyeloscopic examination some form of dysfunction has been revealed; on instituting some medical treatment often a single injection of morphine, eserine, pituitrin, or flavine, the underlying neuromuscular cause of the dysfunction has been disturbed and normal function restored, and the patient is cured and often remains cured. The accompanying chart (Fig. 1) illustrates one such case, the history of which is briefly as follows:

Mrs. F. B., aged 18 years, primipara, was admitted to the Women's Hospital, Melbourne, on April 7, 1930, suffering from eclampsia, she having had 8 fits before admission. She had one convulsion after admission. She received conservative treatment and was delivered 4:15 a.m. on April 9. On April 15 her temperature was 103 degrees F., pulse 128, and she complained of marked tenderness in the right loin. Urinalysis disclosed acid reaction and the presence of pus which contained bacillus coli communis on culture. Patient was put on citrates and the usual medical treatment for pyelitis, but without relief. On April 21, 1930, pyeloscopy was done and disclosed dysfunction of the kidney pelvis and ureter, dilated upper calyx, spasm of long communicating channel from upper calyx, and relaxation of channel to lower calyx, marked antiperistalsis in upper ureter with great pain, not relieved by injection of morphine ¼ grain. She was relieved in 10 seconds by injection of 1 cubic centimeter of pituitrin with restoration of normal kidney pelvis and ureter action. Patient has been quite well since.

The fact that the mere passage of the ureteral catheter did not relieve the condition is to be noted nor did an injection of morphine, but an injection of pituitrin was specific in this case.

In observing the contractions of the kidney pelvis the thought continually obtrudes itself:

Fig. 2. Action of quinine.

Fig. 2A. Action of fatal dose of quinine.

"What is happening to the rest of the kidney while these various parts of the pelvis are contracting and relaxing?" One must recognize, of course, that the kidney is not enclosed in an absolutely rigid membrane; otherwise, naturally, the records obtained in the experimental animal when the kidney is placed in an oncometer would not be possible. This was investigated and will be referred to later. Again, "What happens at the orifices and ends of the collecting tubules when the calyces contract?" Do the active contraction and relaxation of the calyces and the efficient emptying of the pelvis facilitate the passage of urine from the collecting tubules and thus indirectly increase the quantity of urinary flow, and on the other hand does sluggishness of this musculature impede the urinary outflow from the

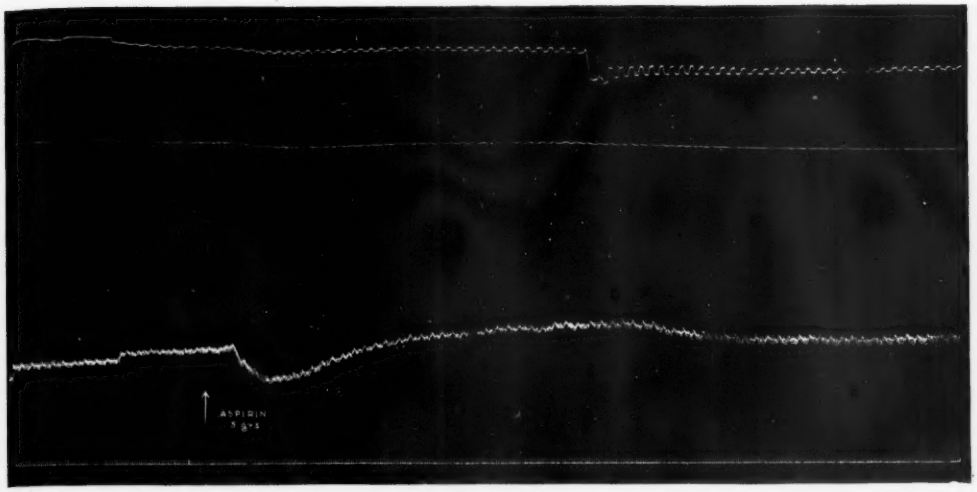


Fig. 3. Action of aspirin.

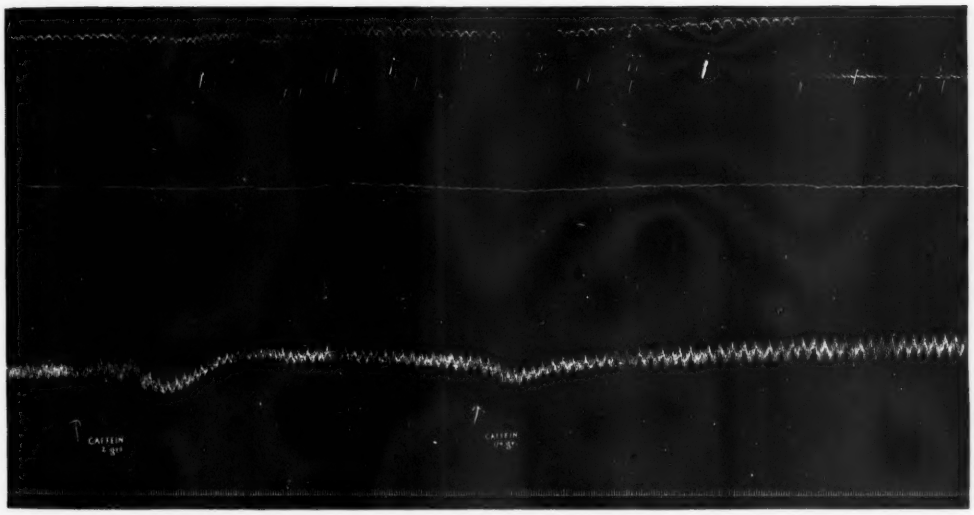


Fig. 4. Action of caffeine.

collecting tubules and thus diminish the total amount of urine produced? Is the diuresis induced by some drugs, such as pituitrin or caffeine, accounted for in this way? Does the activity of the pelvic musculature and the muscularis spiralis papillæ of Muschat so rhythmically affect the renal circulation as actually to influence the amount and degree of the vascular "pulsation" in the kidney in the same way as the respiratory movements affect the flow to and from the heart, or does it act simply by mechanically facilitating the removal of the urine and thus increase secretory activity by diminishing the mechanical resistance to secretion ("back pressure")? What conditions, too, predispose to the de-

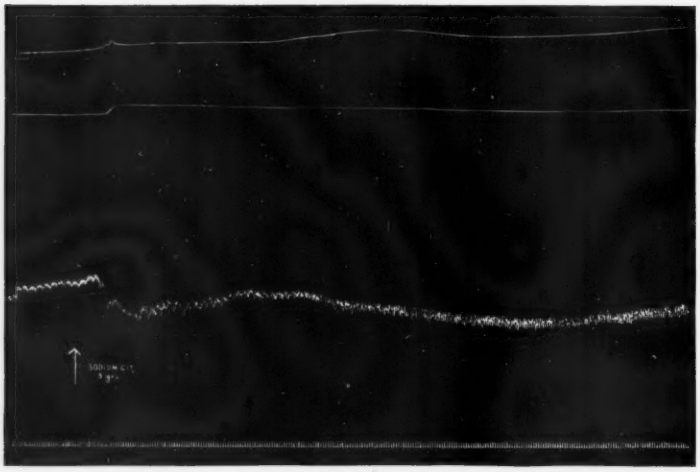


Fig. 5. Action of citrate of soda.

velopment of the various types of dysfunction especially spasm of a communicating channel or ureter, with or without antiperistalsis, and what are the exciting causes? These and many other problems must be investigated from the clinical and experimental sides, both, and the observations herein recorded are an attempt to elucidate some of them.

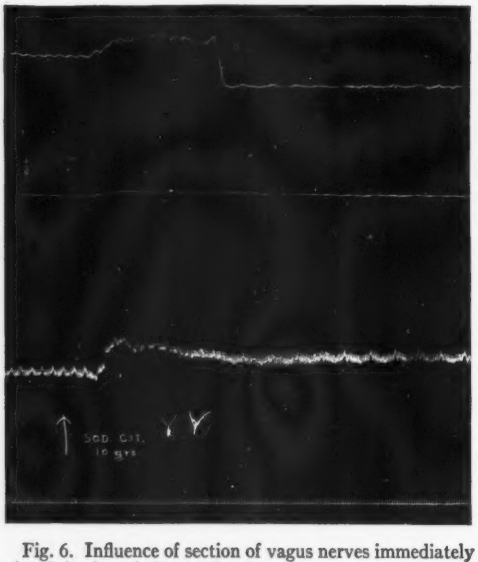


Fig. 6. Influence of section of vagus nerves immediately after injection of citrate of soda.

EXPERIMENTAL

The graphic method described by the author in a former communication (4) was used, but at the same time the kidney was enclosed in an oncometer which registers alterations in kidney volume, which alterations are usually regarded as being due to alterations in arteriolar volume. It will at once be seen from the tracings that although in some cases alterations of kidney volume and renal pelvis volume apparently run parallel, in other cases one sees alterations in kidney volume without apparently any alteration in renal pelvis volume and vice versa, but still one feels that occasionally the one may be a disturbing element in the faithful recording of the other and wherever possible experimental conditions were set up aiming at eliminating disturbing factors.

Drugs. The actions of various drugs were investigated, some on account of their known diuretic action and others for special reasons. From time to time certain drugs have been held up as being specifics for pyelitis when intravenously injected, and more recently mercurochrome and acriflavine have had a vogue here. The drugs are excreted in the urine and are supposed to exert a direct antiseptic action on the urine in the kidney pelvis. From the small doses used one has felt that after injection the dilution in the blood and

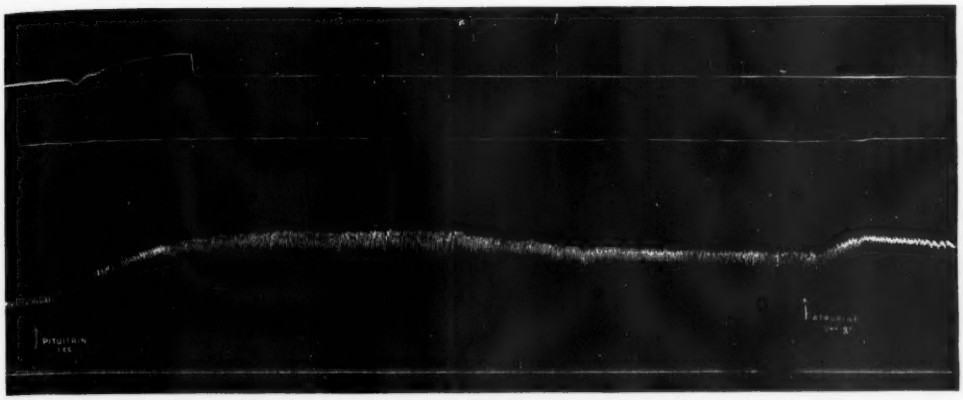


Fig. 7. Action of pituitrin. (See also Fig. 8A.)

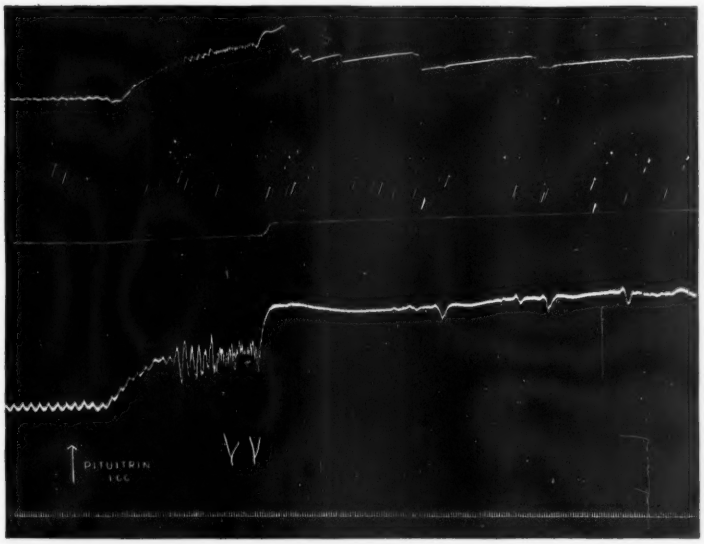


Fig. 7A. Effect of section of vagus nerves after injecting pituitrin.

urine are so great that there can be no question of any antiseptic action and that therefore any beneficial action due to these drugs has been due to some local physiological action. As will be seen later, both these drugs have a histamine-like action due either to their liberating a histamine type of body in the circulation or having a histamine type of action in themselves.

The drugs which were investigated were: quinine, aspirin, caffeine, sodium citrate, pituitrin, eserine, atropine, adrenalin, histamine (ergamine), acriflavine, mercurochrome. The effects of section of the vagus nerves on the action of certain drugs was also investigated.

EXPERIMENTAL RESULTS

Synchronous tracings of blood pressure, kidney volume (oncometer), and contractions of the kidney pelvis were taken. The animals used were medium sized dogs which had received an injection of 4 grains of morphine

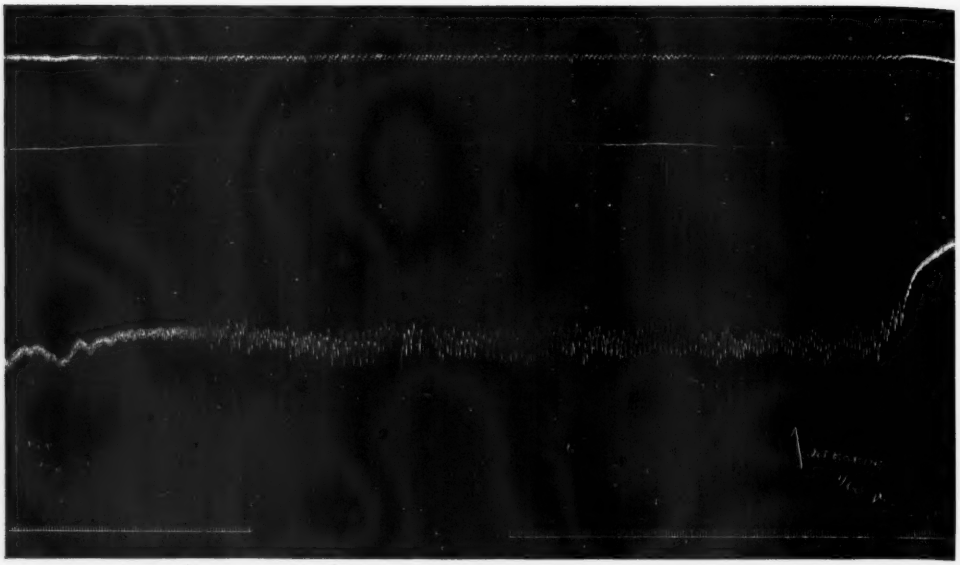


Fig. 8A. Action of

prior to the experiment and were kept under chloroform anæsthesia during the experiment and were killed at the end of the experiment while still under the influence of the anæsthetic. In the tracings three recordings are shown. The lowermost is the blood pressure recording and shows oscillations due to the individual heart beats and respiratory movements. Upward movement indicates a rise in blood pressure and downward a fall. The middle tracing records the changes in volume of the kidney pelvis. Upward movement indicates contraction of the pelvis and downward means relaxation. The uppermost tracing is the oncometric recording of kidney volume and indicates arteriolar volume, vasoconstriction being indicated by a downward movement and vasodilatation by an upward movement. At the bottom of the tracing time is marked in seconds. On the kidney pelvis recording rhythmic waves are sometimes seen apparently synchronous with the respiratory movements, but occasionally the rhythm was slower or faster than the respiratory. These waves have been taken as due to peristaltic or rhythmic waves in the kidney pelvis. In two tracings (Figs. 2A and 9A) they persist after the blood pressure has fallen to zero, and heart beat and respiration are both stopped.

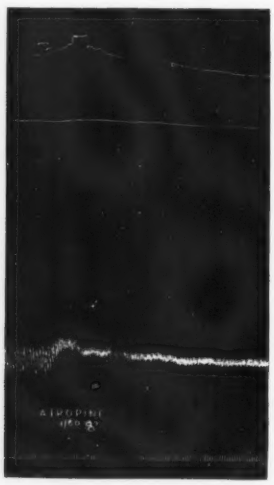
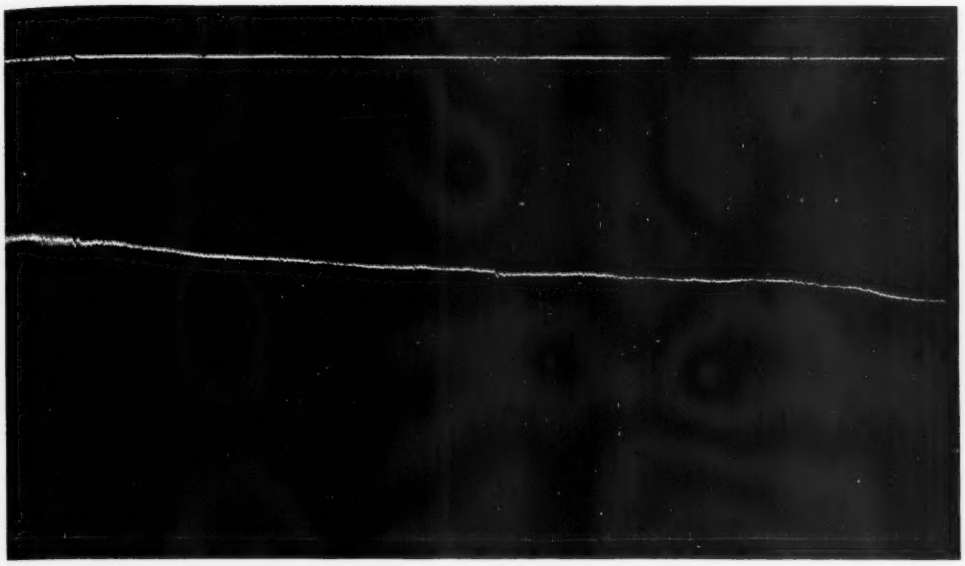


Fig. 8. Action of atropine—pharmacological cutting out of vagi. (See also Fig. 6.)

Quinine (Fig. 2) produced, in the dose given in the tracing, a fall in blood pressure with slight effect on the kidney vessels, but a definite relaxation of the pelvis of the kidney with a lengthening of the inter-



atropine after pituitrin.

val between the peristaltic waves of the pelvis. These waves persisted even when the animal died and the blood pressure had fallen to zero and the animal's heart beat and respirations had ceased (Fig. 2A).

Aspirin (Fig. 3) produced a slight fall in blood pressure with no apparent effect on kidney vessels. The pelvis showed slight relaxation with increase in amplitude of the rhythmic contractions. (In the human being, when the kidney pelvis is being examined with the fluorescent screen a general slowing up of the peristaltic waves is seen in cases in which the pelvis is contracting vigorously and quickly.)

Caffeine (Fig. 4) produces a slight rise in blood pressure while the kidney volume remains practically unaltered, but the kidney pelvis shows a definite

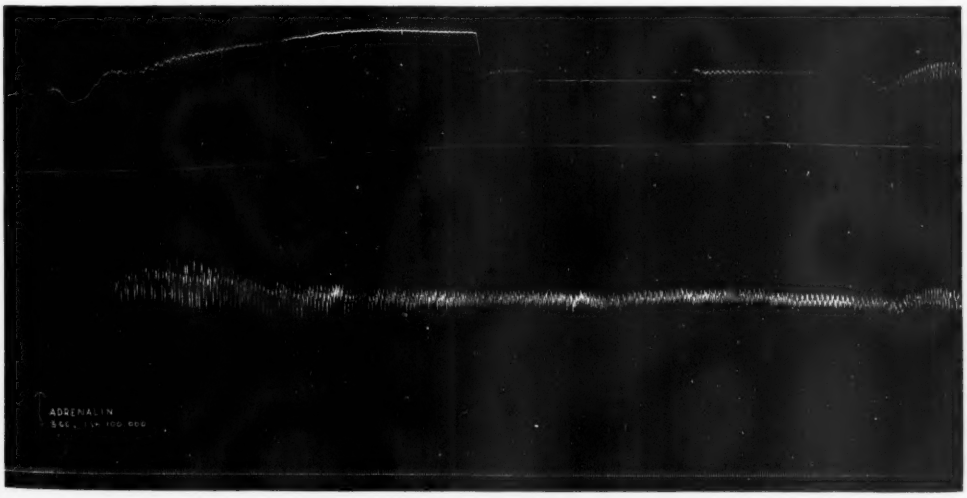


Fig. 9. Action of adrenalin.

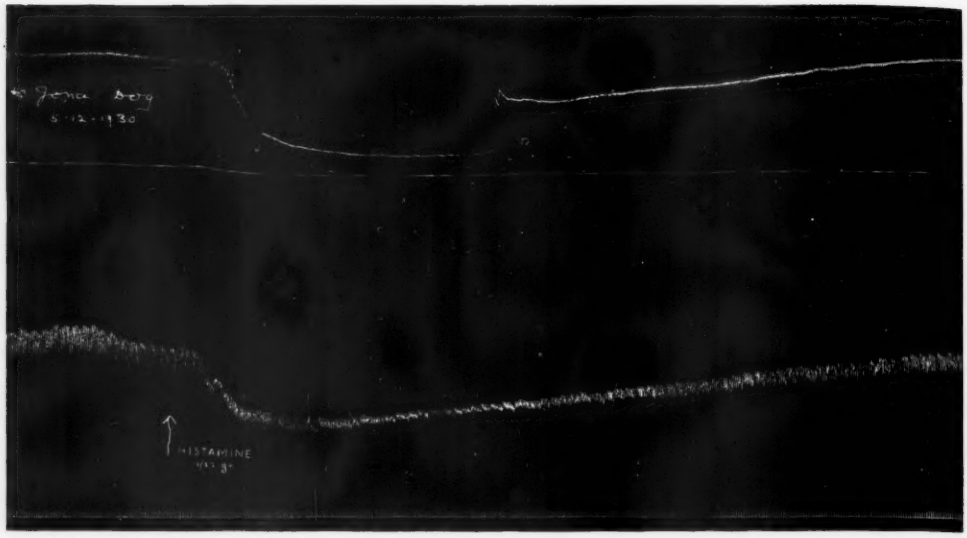


Fig. 10A. Action of histamine showing effects on blood pressure and kidney pelvis, with and without effects on kidney volume.

sustained contraction with marked increase in the amplitude of the peristaltic waves. This effect is more marked with a dose of ¼ grain of caffeine than with a 4-grain dose and disappears after the injection of quinine.

Citrate of soda (Fig. 5) produces a slight vasodilatation with fall in blood pressure but a definite sustained contraction of the kidney pelvis with increase in amplitude of the peristaltic waves. The contraction of the pelvis is maintained for a much longer period when the vagi are cut after the injection of the citrate (Fig. 6).

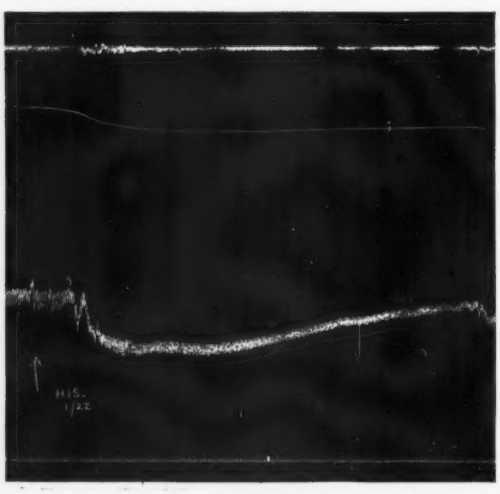


Fig. 10.

Pituitrin, as described in previous papers (3, 4), causes contraction of the pelvis of the kidney and a hurrying of the peristaltic waves in the pelvis and down the ureter. This latter effect is shown in Figure 7. The usual effect on the blood pressure is shown. Clinically in cases in which there is dysfunction, e.g., as in the case of the patient F. B. quoted above, a single dose of pituitrin is often sufficient to correct the dysfunction and re-establish normal function.

Eserine causes contraction of the kidney pelvis.

Atropine in the human being causes a definite relaxation of the kidney pelvis often accompanied by pain which is relieved by morphine, eserine, or pituitrin which induces a contraction. In the dog, however, a contraction is sometimes apparently obtained but this is possibly due to the release of some pressor action, but further work on this point is necessary. Its chief action appears to be the cutting out of vagal control which seems to be a real thing in the dog for when the vagi are cut or atropine injected immediately after an injection of, say pituitrin or sodium citrate, a marked increase in the contraction is produced (Figs. 6 and 8).

Adrenalin causes a steady contraction of the pelvis coming on long after the blood pressure has reached its maximum and lasting long after the blood pressure has come back to normal (Fig. 9).

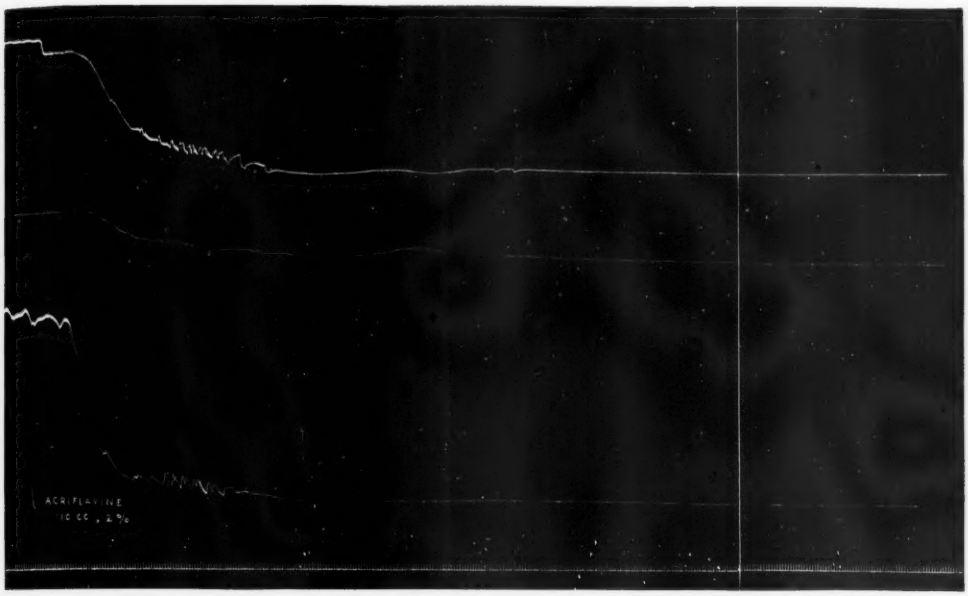


Fig. 11A. Action of fatal dose of acriflavine. Note contractions of kidney pelvis after death of animal. (White line indicates break in chart.)

Histamine (Fig. 10) produces a fall in blood pressure, a passive or secondary constriction of kidney vessels often being associated with the fall in blood pressure and at the same time a relaxation of the kidney pelvis. Numerous tracings obtained demonstrate that these two latter phenomena are quite independent of one another and that the movements of the writing lever attached to the pelvis of the kidney are in no way parallel to and are quite independent of the movements of the writing lever attached to the oncometer.

Acriflavine (Fig. 11). Five cubic centimeters of a 2 per cent solution of acriflavine (i.e., 0.1 gram acriflavine) gives a tracing practically identical with that produced by 0.003 gram histamine (ergamine), but slightly less potent.

Mercurochrome (Fig. 12). Fifteen cubic centimeters of a 5 per cent solution of mercurochrome (i.e., 0.75 gram mercurochrome) gives a tracing practically identical with that produced by 0.003 gram histamine, but somewhat less potent.

As regards vagal control, the tracings obtained after section of the vagi or injection of atropine certainly suggest that the vagus exerts an inhibitory action on the contractility of the kidney pelvis musculature.

An interesting feature noted was that the kidney enclosed in the oncometer failed to secrete urine although the urinary flow was definite both before the kidney was placed in the oncometer and after it was removed. This leads one to think naturally of the operation of decapsulation of the kidney performed with

Fig. 11. Action of acriflavine.

Fig. 12. Action of mercurochrome.

at least temporary success in some cases where the kidney fails to secrete.

RESULTS

The various activities taking place in the kidney are very complex. Not only have we the phenomena of filtration and secretion and re-absorption in the various "essential" parts of the kidney, but the vascular phenomena are also complex, the most important being the rhythmic flow of blood through the kidney by variations in the pressure of the outflowing blood in the renal vein—this rhythmic flow being recognized as also essential to the secretion of urine, the mere maintenance of a head of pressure in the renal artery and an outflow from the renal vein though sufficient for secretion is not adequate for normal purposes (2). In addition to all this we have the rhythmic activity of the musculature of the pyramids, calyces, communicating channels, and body of the pelvis. The whole kidney being contained in a more or less but not absolutely resistant and inelastic capsule one is held by the innumerable possibilities of action and interaction. The demonstration of the action of various drugs not only on the condition of tone or degree of contraction or relaxation of the kidney pelvis and its various parts but the effect of these various drugs on the rhythmic activity of this musculature opens up many possibilities. Two drugs in particular stand out, sodium citrate and caffeine. One has always felt that the diuretic action of citrates was due in large measure at least to the hydræmic plethora induced, while the action of caffeine was supposed to be some obscure specific action on the secreting cells of the kidney. While we may still regard these modes of action as true, the direct action on the musculature of the collecting system from the pyramids to the ureter with a "milking" effect may be quite a considerable factor in determining the diuretic action of these drugs. The action of those drugs, also, which induce or stimulate peristalsis or facilitate emptying of the renal pelvis either by contraction of the pelvis such as pituitrin or eserine, by increasing the peristaltic waves such as caffeine and sodium citrate or by inducing a measure of relaxation in some part of the collecting system musculature which is in a condition of spasm and ensuring uninterrupted peristalsis with free outflow of urine such as would be induced by histamine, mercurochrome, and acriflavine in appropriate dosage—all these actions must produce a decidedly beneficial effect in those cases where there is backworking or stagnation of urine in the collecting system. Pyeloscopy determines some such dysfunction in cases of pyelitis and in many cases of obscure kidney pain, and once the underlying pathological process has been determined all that is necessary to cure the condition is the exhibition of the appropriate drug in the optimum dose to restore normality. The optimum dose is certainly a point to be considered as overdosage may be just as prejudicial to a successful result as faulty diagnosis or incorrect therapy, the correct dose being one which will, say, cause sufficient relaxation to relieve spasm but not sufficient to cause dilatation of the pelvis with backworking and exaggeration of symptoms. This latter will no doubt explain some of the failures obtained with forms of therapy which had proved successful in other cases of similar type. One certainly recommends that the therapy to be followed should be determined so far as possible while the kidney is being observed under the fluorescent screen. The very definite and

marked effect of histamine raises many problems in the pathology of renal pain. One has seen renal pain, severe and resistant to all forms of treatment and yet associated with apparently no other abnormality than a mild bacilluria, generally bacillus coli communis. Whether the bacillus coli communis or any other organism has the power to liberate histamine-like bodies locally or whether they are formed elsewhere and, passing through the circulation, only exert an action on the kidney as part of their general action remains to be proved. The common association of bowel trouble, most commonly constipation, with pyelitis is recognized, as also is the difficulty sometimes experienced in the differential diagnosis of right sided pyelitis from gall-bladder or appendical trouble. The history comes to the author's mind of one patient who came to him still complaining of a deep seated, right sided pain after having had three operations—appendicectomy, then gall-bladder drainage, and then cholecystectomy—and in whom pyeloscopy determined spasm of a very long communicating channel from the upper calyx. She was cured by eserine. The association of the pyelitis with toxæmia, pyrexia, and shivering suggest that a common factor is at work in regard to the causation of the local renal dysfunction and the general symptoms. The author some years ago (5) demonstrated that the "pyrogen" which was isolated from broken-up bacteria and which produced pyrexia when injected into the experimental animal was a relatively simple body of the amine type on a fatty acid basis, and was apparently related to histamine, which was discovered and so thoroughly worked out by Dale and his collaborators (1). In this connection the work of Koessler and Hanke (6) is suggestive. These authors have shown that bacillus coli communis will convert histidine (a 6 carbon degradation product of protein) into histamine in the presence of glycerine or glucose and a source of nitrogen (the nitrogen and the glucose or glycerine being essential). The conditions found in the bowel would certainly comply with these requirements especially where conditions of bacterial fermentation of undigested foodstuffs exist. A vista of further possibilities and speculations is opened up by this work but a discussion on these lines would be out of place and unnecessary here as it is merely the author's desire to attract the attention of the practical clinician to the value of pyeloscopy as an aid to diagnosis and therapy in this branch of abdominal medicine. Further work is being done from the clinical side in the direction of obtaining graphic records of the activity of the human kidney pelvis. For this work we are using an apparatus, slightly modified, but on the lines of that used in the experimental work here described, and it is hoped to publish the results of this work in due course.

I desire to express my thanks to Professor W. A. Osborne for the use of his laboratories and facilities.

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Postoperative Latent Jaundice—Norman W. Elton.

POSTOPERATIVE LATENT JAUNDICE[1]

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Assistant in Medicine, Boston University School of Medicine

DURING a survey of the incidence of latent jaundice, icteric Wassermann sera were routinely examined for a period of 7 weeks at St. Mary's Hospital, Detroit, Michigan, by the use of the icterus index, van den Bergh reaction, and quantitative serum bilirubin determination. Sera were selected because they appeared more yellow than normal. Almost invariably latent jaundice was encountered in such sera by one or all of the three tests, representing about one out of eight of the sera routinely taken for the Wassermann test. Two hundred sera were thus examined and the records of the patients carefully studied.

About 75 of these sera were taken from patients admitted because of accidental trauma, or from patients who had just returned from the operating room. The remainder were from patients with lobar pneumonia; pernicious anæmia; recognized and unrecognized familial jaundice; septicæmia; cardiac failure (rheumatic or luetic etiology); acute upper respiratory infection; acute follicular tonsillitis; peri-tonsillar abscess; acute salpingitis; acute epididymitis; extravasation of urine; diabetes mellitus; carbon monoxide, carbon tetrachloride, lead, and iodin poisoning; hepatic cirrhoses; alcoholism; cerebral hæmorrhage; metastatic carcinoma of the liver; carcinoma of the head of the pancreas; acute cholecystitis; duodenal ulcer; infectious ("catarrhal") jaundice; pernicious vomiting of pregnancy; thrombo-angiitis obliterans; incomplete abortion; and a few from the cords of the newborn.

Charts 1 to 20. On these charts there are three curves. The upper curve is invariably that of the icterus index, the middle curve that of the quantitative bilirubin, with their scales as indicated at the left. At the bottom the van den Bergh reaction curve is plotted in terms of its delay period, a dot on the "direct" line indicating the direct positive reaction. The delay period scale is in minutes. A circle on the "direct" line indicates the presence of an immediate golden reaction when the reagent mixes with the serum. An "N" at the bottom indicates that the direct reaction was negative up to 10 minutes. "O" day is the day of operation, blood being taken immediately on return from the operating room.

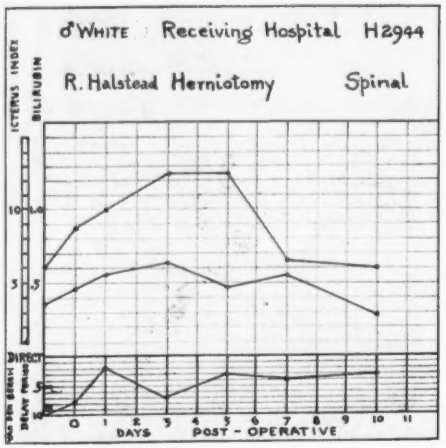
The technique used for the icterus index was the colorimetric method described by Bernheim; for the van den Bergh reaction, that of its originator; for the quantitative bilirubin, the modification developed by Thannhauser and Anderson. The normal icterus index was considered to be from 3 to 5 with satisfactory sera, and the normal bilirubin content below 0.2 milligrams per 100 cubic centimeters of serum (6). As for the van den Bergh reaction and its interpretation, it was deemed advisable to revert to the terminology described by van den Bergh himself in his recent re-issue of *Der Gallenfarbstoff im Blute*, rather than to attempt to sort out the confusing array of conflicting ideas from other sources.

In contusions, fractures, deep lacerations, bullet wounds, operative incisions, cerebral hæmorrhage, and ruptured ectopic pregnancy an interstitial blood extravasation is a common factor. One cubic centimeter of blood alone contains approximately 140 milligrams of hæmoglobin from which an appreciable quantity of hæmatoidin may be formed. Rich has pointed out that this hæmatoidin is formed at the site of the extravasation and is, so far as is known, identical with bilirubin. Hence, in all of these conditions it may be assumed that an excess of bilirubin is formed and released into the blood stream to be excreted by the liver. Latent jaundice following the rupture of ectopic pregnancy is well known (3), and the latent jaundice of true cerebral hæmorrhage has been demonstrated by Wilder, and again by Cheney. Latent jaundice also results from traumatic interstitial blood extravasation (1), as indicated on the accompanying table and charts.

Table I exhibits the findings in a representative group from 63 cases found by the examination of Wassermann sera during a period of 7 weeks at St. Mary's Hospital, Detroit, Michigan. A wide variety of accidental lesions without any organic disease is represented. It is to be noted that direct

[1]Work done in the Department of Pathology, Detroit College of Medicine and Surgery, 1929–1930.

Postoperative Latent Jaundice—Norman W. Elton.


♂ WHITE Receiving Hospital H2944
R. Halstead Herniotomy Spinal
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

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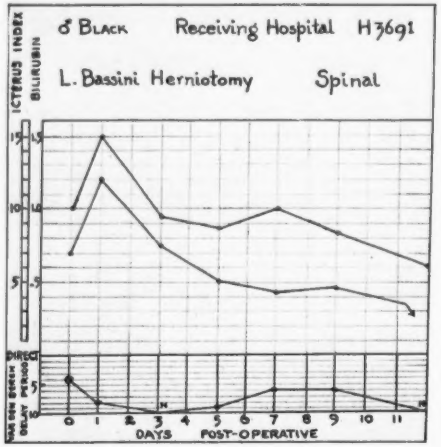
♂ BLACK Receiving Hospital H3691
L. Bassini Herniotomy Spinal
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

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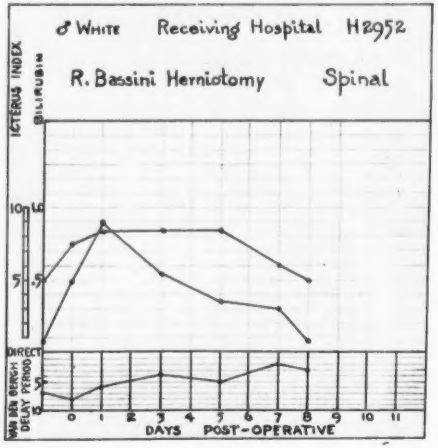
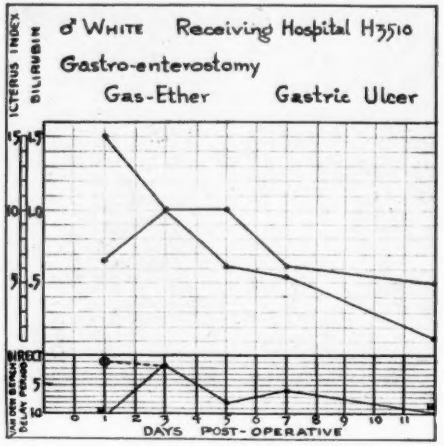
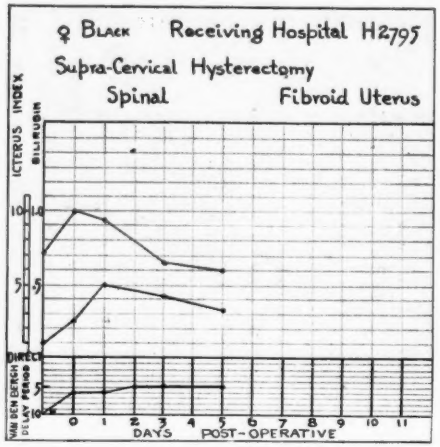

♂ WHITE Receiving Hospital H2952
R. Bassini Herniotomy Spinal
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

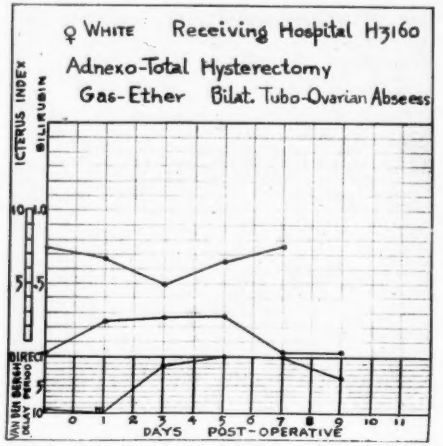
9.


♂ WHITE Receiving Hospital H3510
Gastro-enterostomy
Gas-Ether Gastric Ulcer
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

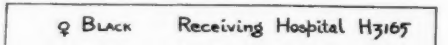
10.


♀ BLACK Receiving Hospital H2795
Supra-Cervical Hysterectomy
Spinal Fibroid Uterus
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

11.


♀ WHITE Receiving Hospital H3160
Adnexo-Total Hysterectomy
Gas-Ether Bilat. Tubo-Ovarian Abscess
ICTERUS INDEX
BILIRUBIN
DIRECT
VAN DEN BERGH DELAY PERIOD
DAYS POST-OPERATIVE

12.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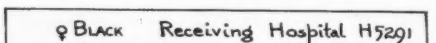
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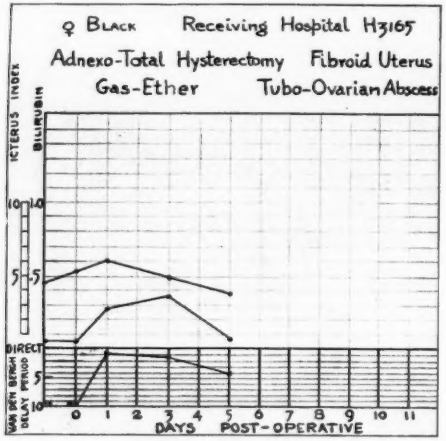

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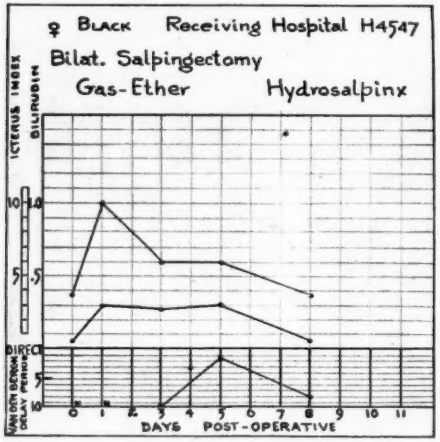

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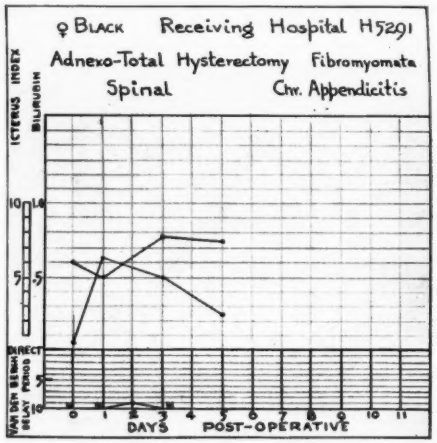

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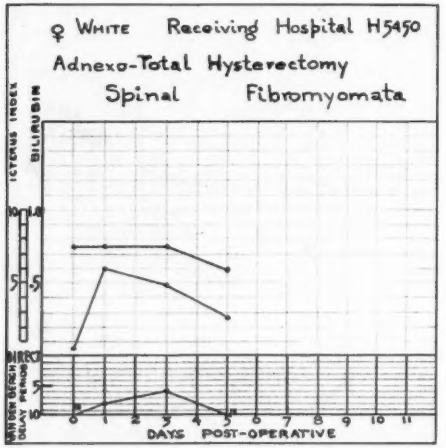

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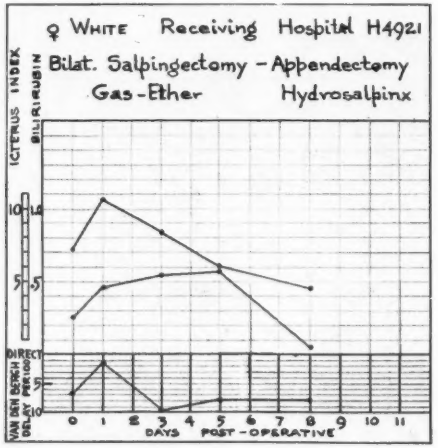

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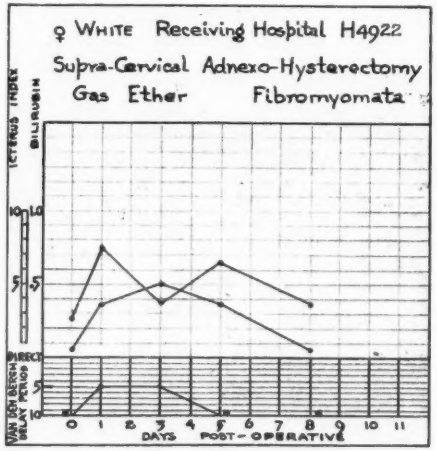

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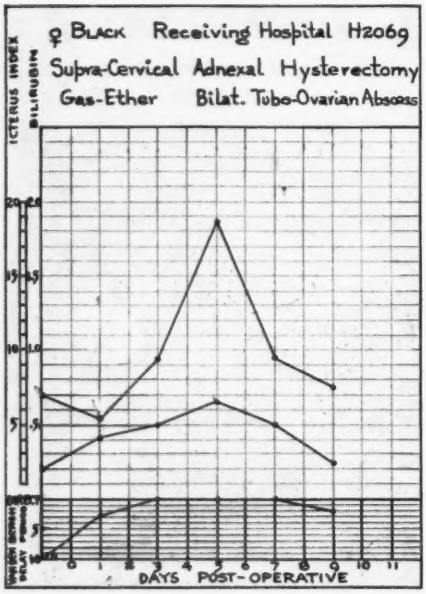

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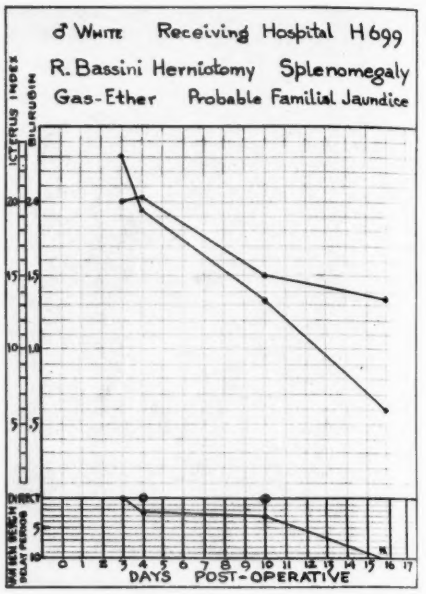

20.

positive van den Bergh reactions were not uncommon, that very short delay periods in the reaction were common, and that immediate zonal reactions, obtained by overlaying the diazo reagent on the serum prior to mixing, were quite common.

Charts 1 to 20 show the curves in latent postoperative hæmatoidin icterus.

TABLE I.—TRAUMATIC CASES*

Series No.	Site	Day post-trauma	Icterus index	van den Bergh reaction	Quantitative bilirubin
	FRACTURES				
1	Rib	2	7.5	Delayed 5 min	.7
2	Ribs-patella	0	12.5	Delayed 5 min	1.5
3	Ribs	1	10.8	Delayed 1½ min	.54
4	Skull, died	1	11.6	Delayed 6 min	.71
5	Femur	1	12.5	Delayed 12 min	.2
6	Femur	0	15.5	Delayed 5 min	.92
7	Femur-tibia	0	15.5	Delayed 5 min	1.7
8	Humerus	3	10.0	Delayed 3 min	.9
9	Tibia-fibula	5	15.0	Delayed 5 min	.75
10	Scaphoid cuboid gangrene	11	8.3	Delayed 8 min	.6
11	Rib	1	10.0	Delayed 4 min	.9
12	Pott's	2	18.7	Direct	1.1
13	Ribs	2	10.0	Zonal D1½	.7
14	Pelvis	1	10.0	Delayed 4 min	.6
15	Humerus	0	7.9	Delayed 3 min	.66
16	Ribs-fibula	2	8.8	Delayed 2½ min	1.5
17	Pelvis	0	8.8	Delayed 2 min	.73
18	Ilium	1	10.0	Zonal D2	.7
19	Skull, died	0	5.0	Delayed 10 min	.39
20	Wrist	0	13.6	Zonal D3	1.07
21	Femur-path	2	6.8	Delayed 8 min	.3
22	Femur	1	10.0	Zonal D2	.41
23	Pott's	10	8.3	Delayed 7 min	.66
	CONTUSIONS				
1	Chest	3	7.5	Delayed 4 min	.55
2	Chest	1	10.0	Direct	.79
3	Elbow	2	15.0	Delayed 7 min	1.03
4	Scalp	1	10.7	Delayed 15 min	1.15
5	Multiple	3	7.5	Zonal D1½	.47
6	Scalp	3	16.6	Delayed 4 min	2.6
7	Scalp	1	15.0	Delayed 5 min	.85
8	Face	0	13.6	Delayed 5 min	1.1
9	Scalp	1	10.7	Delayed 10 min	.9
10	Scalp	0	10.7	Delayed 6 min	.8
11	Scalp	1	8.0	Delayed 12 min	1.0
12	Scalp	0	13.7	Zonal D1½	.8
13	Scalp	1	10.0	Delayed 4 min	1.1
14	Orbit	3	12.5	Delayed 4 min	.67
15	Scalp	1	15.0	Delayed 15 min	.64
16	Orbit	4	8.8	Delayed 12 min	.36
17	Scalp	6	12.5	Delayed 12 min	.8
18	Scalp	2	15.5	Delayed 3 min	.69
19	Face	1	5.5	Delayed 10 min	1.08
20	Face	0	13.6	Direct	.86
	DEEP LACERATION				
A	Arms	3	12.5	Golden direct	1.1
	BURN				
B	Arm-Buttock 2°.	0	10.0	Delayed 4 min	.8
	BULLET WOUND				
C	Buttock	0	7.9	Delayed 8 min	.5

*The site of the trauma is given; the day after the injury on which the blood was taken is indicated (an O signifies that the specimen was taken on the day of the injury); in the column for the findings in the van den Bergh reaction, with the letter D is noted the delay period in the direct reaction on mixing after the development of an immediate zonal reaction.

Fifty patients were observed after operation, all of whom exhibited some degree of latent jaundice in one or all of the three tests, except in an occasional hæmorrhoidectomy. Twenty of these were studied serially with the three tests and are charted. Zonal positive reactions were usually immediate if the delay period in the van den Bergh reaction after subsequent mixing was 2 minutes or less, but are not recorded on the charts. The striking feature of these charts is that although the liver function of these patients, as well as of those suffering from accidental trauma, can hardly be regarded as impaired, there is evidence of a definite direct positive tendency in the van den Bergh reaction during the excretion of the overload of bilirubin. The nature of the anæsthetic used was quite irrelevant. No chloroform was used. The amount of pigment to be excreted as well as its rate of release undoubtedly varied somewhat, dependent on the type of incision made, the extent of the extravasation, and the relative vascularity of the area involved. Frank direct positive reactions are shown in Charts 12, 19, and 20. Immediate zonal reactions were present at the time of the short delay periods on Charts 2, 3, 14, and 17. All charts exhibit more or less the direct positive tendency. Chart 20 exhibits the development of a direct positive reaction on the third day after operation in a case of familial jaundice recognized only after herniotomy, and maintaining an anomalous immediate direct golden reaction until the tenth day.

SUMMARY

Latent icterus develops following trauma, accidental or operative, probably due to the release of a surplus of bilirubin from the interstitial blood extravasation. In a study of 20 consecutive patients undergoing an uneventful postoperative recovery after a wide variety of operations in whom either general or spinal anæsthesia was used, it is found that there is evidence of a definite direct positive tendency in the van den Bergh reaction that is difficult to explain by any known pathological process in the liver, and which appears to be associated only with the excretion of a surplus of bilirubin.

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THE COMMON BILE DUCT[1]

JOHN B. DEAVER, M.D., AND V. G. BURDEN,[2] M.D., PHILADELPHIA

THE surgical treatment of disease of the biliary tract, in the past and present, has been concerned chiefly with affections of the gall bladder. In this period of 50 years, there has been ample time and experience to evaluate results. It has been the privilege of the senior author to be an active participant throughout this half century of surgical progress. In retrospect, on contemplation of the good and evil in this special field of surgery, there stands out with the prominence of indelible memory the rôle of the common duct. It requires much bitter and trying experience adequately to appreciate the importance of the common duct in the satisfactory and unsatisfactory results of surgery of the biliary tract. Unlike the gall bladder the common bile duct is indispensable, yet it is so readily affected by disease and operative trauma, the consequences of which are often disastrous, that its surgical importance scarcely can be overestimated.

Anatomically, the common bile duct lies in the right free border of the gastrohepatic omentum, then behind the duodenum, between the duodenum and the pancreas or in a groove in the head of the pancreas whence it enters the wall of the duodenum through which it passes obliquely to its terminal opening, the papilla of Vater, surrounded by the sphincter of Oddi. The first or supraduodenal portion is not always present for the reason that in some instances the hepatic duct is prolonged down to the outer border of the duodenum before it is joined by the cystic duct. The supraduodenal portion of the duct in the gastrohepatic omentum is accompanied by the hepatic artery and portal vein and by several lymphatic glands external to the omentum. The intimate relationship between the duct and nearby structures—the gall bladder, the pylorus, the duodenum, and the pancreas—makes it subject to mechanical and infectious derangements consequent upon disease of these organs.

From its gross appearance, the common duct appears to be a passive channel for the transit of bile. In view of the surgical importance of the duct, a detailed description of its finer anatomy should be of value. But such cannot be found in modern textbooks of anatomy. The older anatomists described glands in the walls of the extrahepatic bile ducts. The presence of muscular tissue has been disputed. Burden carried out microscopic studies on the extrahepatic ducts of the human subject and gave a description of the surgical histopathology. When the common duct is laid open the internal surface presents a characteristic appearance and at first seems to be reticulated, but on closer inspection under the dissecting microscope, it is seen to be covered by minute pits or shallow depressions, some of which contain plugs of mucus. Cross sections of the duct show a lining layer of tall columnar epithelium not unlike that which covers the rugæ of the gall bladder. Beneath the lining layer is a thick compact layer of connective tissue which contains considerable elastic tissue. The outer layer of the duct wall is composed of loose areolar tissue in which are found blood vessels, lymphatics, and muscle. The muscular layer is composed of good sized, isolated, oval bundles of unstriped fibers, some of which are arranged in a longitudinal and others in a circular direction. The pits which appear on the internal surface of the duct are mere shallow epithelium-lined depressions between folds of mucous membrane. Adjacent to the lumen of the duct and opening into it are ampulla-like cavities lined with epithelium. Into these cavities drain the ducts of mucous glands which are found richly distributed throughout the wall of the common duct. The glands in the wall of the duct are of particular interest since it was found that in patients who had cholecystitis the glands constantly showed inflammatory changes characterized by surrounding round-cell infiltration and cystic changes. The

[1] Read before the Detroit Academy of Surgery May 13, 1931, Detroit Michigan.
[2] By invitation

surgical significance of these findings in the wall of the common duct is important in their bearing on the sequelæ of biliary tract infection. An infection so situated is difficult to eradicate and the consequences may seriously jeopardize the integrity of the main bile channel. Thus it appears that choledochitis does not merely express or signify a catarrhal condition of the lining of the bile duct.

Some of the gross lesions affecting the common duct are stone, stricture, ulceration, and neoplastic growths. It may also be involved by infection and adhesions extending from adjacent structures as the gall bladder, duodenum, pancreas, and regional lymph glands.

The location of the duct and its topographical relations make the part it plays in biliary tract infection highly important. The third part, the pancreatic, and the fourth, the interstitial, are its most important portions. The terminal portion is dilated, forming the ampulla of Vater and terminates as the papilla of Vater surrounded by the sphincter of Oddi, making it the more important of the two latter portions. This has been shown more particularly in the last few years, during which time more operations have been done for biliary tract infection, thus offering greater opportunity for the better interpretation of the pathological findings; and also since biliary tract drainage by duodenal tubage has occupied a prominent place in the medical treatment of biliary tract infection. We refer particularly to the influence which the sphincter of Oddi has upon the drainage of the common duct and the filling of the gall bladder, and the part it plays in the pathology of the duct.

Other pathologic conditions found in the common duct are inflammation (choledochitis), stricture, ulceration and perforative ulceration, stone, distention with muddy, sandy bile, neoplastic growth and diverticulum, which if large, results in cystic dilatation of the duct. The traumatic conditions include section, tear, or removal of a portion of the wall and ligature, all of which, if not recognized at the time of occurrence and repaired, result in a bile fistula or permanent jaundice. Any one of these conditions may result in failure of the original operation to give relief. Further, they leave the patient worse off than before the operation. Although the traumatic conditions may occur in the hands of the most expert surgeon, nevertheless they are an insult to surgery and decidedly detract from the sum total of beneficial results.

Let us next analyze the pathologic and traumatic conditions. Inflammation of the common duct in the majority of instances is a result of cholecystitis. The second most common cause, a contributory one, is stone in the common duct, since in almost every such instance there has been an antecedent cholecystitis. The presence of the stone in the duct, because it is a foreign body and because it causes a varying degree of biliary obstruction, acts to intensify the local inflammatory reaction and even may give rise to ulceration.

Inflammation of the duct is recognized through sight and touch by the presence of dilatation, and by opacity and thickening of the walls. The normal duct is about 6 or 7 millimeters in diameter and has a blue color similar to that of the gall bladder. Ordinarily, it cannot be palpated as a separate structure in the gastrohepatic omentum because of its thin collapsible walls. Palpatory examination of the duct is carried out by inserting the tip of the index finger into the foramen of Winslow and gently compressing the overlying structures between the finger and the thumb. When the foramen of Winslow is occluded by adhesions this method of palpation cannot be done satisfactorily unless one is able to define by touch the border of the gastrohepatic omentum. The latter may be thick and indurated and have overlying enlarged lymphatic glands. When in doubt, the duct may be directly inspected by incising the gastrohepatic omentum along its right free border. When the history is suggestive of stone in the common duct it has been our experience that negative palpatory findings are not reliable and we do not feel satisfied until the duct has been opened and its interior examined by touch if possible and by the probe.

Stricture of the common duct is always followed by jaundice which may be intermittent or permanent. In many cases the symptoms cannot be distinguished from those of common duct stone. Where the type of jaundice

is intermittent, the explanation is probably that the stricture has narrowed but not completely occluded the lumen and at certain times by reason of the character of the bile or local inflammatory œdema the pathway becomes obstructed. Occasionally, there is a stone above the stricture. A stricture of this type may exist for years. When the stricture is complete, jaundice is permanent unless there be a biliary fistula above it. Formerly it was believed that stricture of the common duct was always due to injury, but latterly since many more operations have been done for disease of the biliary tract and there has been more intensive study of the condition of the liver, it is known to be sometimes the result of general obliterative cholangitis. In the absence of traumatism, some cases are probably due to persistent postoperative choledochitis. Nevertheless, operative injury remains as the most potent etiological factor in the condition. The stricture may be a local, annular lesion or it may extend along the greater portion of the duct. Stricture at the terminal end may be difficult to detect unless probes be passed down toward the duodenum.

The glands in the wall of the common duct may harbor persistent infection which spreads by continuity of structure until it becomes widely disseminated along the bile tube. The inflammation in the wall of the duct results in infiltration with leucocytes, deformity and distention of the mucous glands, and the formation of fibrous tissue leading to thickening and rigidity of the duct. Judd and Councellor carried out microscopic studies on the intrahepatic biliary tree and called attention to the fact that general obliterative cholangitis may exist for months before there are signs of stricture of the common duct. Stricture may be the result, as already stated, of cholangitis and ulceration. The pathologic changes result from infection of the glands within the walls of the duct as well as from the presence of stone. A stone that obstructs the common duct and causes proximal retention of bile may lead to ulcerative perforation and escape of bile into the subhepatic fossa. My former interne and your fellow member, Dr. Vale, has related to me such a case occurring in his experience. Distention of the common duct with muddy, sandy bile exposes the walls of the duct to changes which may result in partial obliteration of its lumen. Neoplastic growths may affect the common duct as extensions from carcinoma of the gall bladder or they may occur as a primary tumor of the duct which is most commonly situated at the terminus of the duct in the peri-ampullar region.

Diverticula of the common duct are caused by obstruction in conjunction with a localized weakness of the wall. Rarely, a traction diverticulum may be the result of adhesions. Congenital dilatation of the duct which may reach the size of the small intestine has been encountered in a few reported cases, the causative factor being a diaphragm-like occlusion at the lower end of the duct. The senior author on more than one occasion has encountered a diverticulum of the common duct large enough to constitute a cyst. Injury to the common duct during the course of operation, unfortunately, is not a rare occurrence. It usually affects the portion at the cystic duct juncture. Strong traction on the gall bladder preparatory to removal may angulate the common duct at this point so that if the effort to remove all of the cystic duct be too ambitious the clamp may include a section of the wall of the common duct which will be excised and the applied ligature is then on the side of the main duct. Should the ligature hold and healing occur, a stricture will follow. In case the ligature separates before healing, a biliary fistula is formed. Sometimes the cystic artery escapes the clamp or ligature and retracts behind the main duct. Unless caution is observed in its recapture the hæmostat may be applied to the common duct. Œdema and inflammatory exudate around the neck of the gall bladder and cystic duct make definition of structures difficult. In such instances it is wise to make a high ligation of the cystic duct. The watch-word in surgery of the biliary tract is "see well what you do." This applies particularly to surgery of the common duct. The normal relations of the duct are often distorted by disease so that even the expert is not able to recognize it by sight and touch. Identification of the structure in question often can be made by aspiration through

a long, fine needle attached to a syringe. The aspirate, bile or blood, will distinguish between common bile duct and portal vein, the two structures most readily confused. The surgeon should be acquainted with the more common anomalies of the ducts. By exposing the duct at a point where there is the least amount of pathological tissue, it can be traced upward to the site of operation and handled with comparative safety.

Stricture of the common duct due to cholangitis may not give clinical manifestation for a considerable length of time after the primary operation. Postoperative, intermittent biliary obstruction is always more or less suggestive of stricture. The lesion, essentially, is the result of inflammation and contraction which eventually infringes upon the patency of the lumen of the duct until there are clinical signs of impeded bile flow. In those cases, usually hopeless, of obliterative cholangitis encountered in infants, it may be possible that the inflammation in the biliary tract was caused by toxins from the mother conveyed to the liver of the fetus.

Anatomically, physiologically, pathologically, and surgically, the ampulla of Vater rivals the gall bladder as the most important part of the extrahepatic biliary tract. Anatomically, it is important because of its position in the wall of the duodenum, where it is surrounded by the sphincter of Oddi. The sphincter plays a major rôle in the physiology of bile flow. It restrains the escape of bile into the duodenum until the contractile force of the gall bladder in conjunction with reciprocal innervation overcomes its normal tonus. It is the most important agent in causing the gall bladder to fill with bile. As one of us (V.G.B.) pointed out in a previous paper, the findings of cholecystography should be interpreted in terms of the behavior of the sphincter of Oddi. The most potent factor in the absence of the gall bladder shadow in the cholecystogram is incompetency of the sphincter of Oddi. Pathologically, it is capable of playing a mischievous rôle when the sphincter is in spasm or when the peri-ampullar structures are infiltrated by inflammatory exudate. Judd and Burden described a group of cases in which there was postoperative, non-calculous, intermittent biliary obstruction probably caused by spasm of the sphincter of Oddi. Surgically, under abnormal conditions of persistent contracture or spasm, it figures prominently as an etiologic factor in pancreatic œdema. Especially potent is its influence on the postoperative morbidity of biliary surgery. For years the senior author has called attention to this both by clinical demonstration and by the written page. Regardless of the type of operation on the common duct, whether it be for inflammation, stricture, stone, or neoplasm, it is not complete unless the patency of the duct through to the duodenum has been demonstrated to complete satisfaction. Were it possible to remove half of the sphincter of Oddi as in the removal of the anterior half of the pyloric sphincter for pylorospasm, there would be fewer residual conditions so disappointing to the surgeon and patient. One German surgeon has devised and uses graduated sounds for dilating the sphincter of Oddi. From our clinical experience, we do not believe that experimental data relative to reflux of duodenal contents constitute a major objection to instrumental dilatation of the sphincter. Thoroughness is the keynote in surgery of the common duct. The sequelæ of carelessness mentioned elsewhere are disconcerting legacies. Only by delicate searching and instrumental exploration can one be sure that the papilla of Vater is open unless there be an obstructing stone or neoplasm.

The surgical procedures which have been practiced on the common duct are varied and ingenious. Especially so are those which have to do with restoration of continuity of the main bile channel. The prime motive in all is an uninterrupted passage for bile into the intestine. The resourcefulness of the surgeon is often put to extreme test. These supreme difficulties should be undertaken only by the surgeon of long experience, yet the unsuspected occasion may arise in the practice of the average surgeon. He must be prepared to act to extricate himself and the patient from a trying situation. If the problem cannot be solved at once, an immediate crisis can be averted by providing for an external biliary fistula leaving the final step of the operation

to a time when circumstances are more favorable. The more common surgical lesions of the common duct call for a thorough operative procedure which is conservative in its radicalism.

In the case of the inflamed dilated common duct, incision, exploration, removal of the obstruction, and drainage by the T-tube is the procedure. For the narrow stricture, sleeve resection and closure by end-to-end union, leaving an opening in the anterior wall for the introduction of a T-tube will usually be curative. When the stricture is diffuse, it may be incised and a T-tube inserted or the upper wide portion of the duct may be anastomosed to the duodenum or stomach by an end-to-side junction.

Single or multiple stones in the duct, if not in the supraduodenal portion, should, if possible, be milked back into the upper accessible portion of the duct where they can be cut down upon and removed. Once the stone is within the grasp of the fingers it should not be allowed to escape until removed. If the stone be allowed to slip into one of the branches of the hepatic duct its recovery will be difficult.

When the stone occupies the pancreatic portion, especially the lower part, it is usually situated in a localized dilatation or pocket and its removal is difficult. Only rarely can it be forced into the upper portion of the duct. Several methods to extricate it must be tried. A gallstone scoop may be passed down to it through an opening in the first portion of the duct and by manipulation the stone may be dislodged or broken and removed piecemeal. The stone may be pushed into the duodenum. When all these means fail, the duodenum should be mobilized, turned toward the left, and the duct incised over the stone. Following removal, a T-tube is inserted into the opening in the first portion of the duct in such a way that its lower horizontal limb extends down the duct into the duodenum.

A stone in the ampulla of Vater usually can be pushed into the duodenum, or dislodged and removed above, or broken up with the aid of the scoop in the duct and counter pressure on the duodenum with the tips of the fingers. But all of these may fail and then the only alternative is direct removal through a transduodenal incision. We reserve this procedure as a last resort and only occasionaly have been called upon to use it. It carries the risk of duodenal fistula. Crushing the stone in the duct is a dangerous procedure because of the likely injury to the walls.

In the presence of a new-growth, its location, size, and type, usually malignant, will guide the operator in deciding what is best to do.

Impassable or irremovable obstructions of the common duct are rarely encountered at primary operation on the biliary tract. If such be the case, with an intact gall bladder and a patulous cystic duct, then cholecystogastrostomy is the operation of choice.

In conclusion it may be stated that any discussion of the surgery of the common duct must take into consideration its normal and pathological histology, the fact that its lesions usually represent complications of disease of the gall bladder and therefore are preventable by timely surgery.

CLINICAL SURGERY

FROM BRONCHOSCOPIC AND SURGICAL CLINICS, TEMPLE UNIVERSITY

THE SINGLE STAGE OPERATION FOR PULSION DIVERTICULUM OF THE ŒSOPHAGUS

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IN the Bronchoscopic Clinic more than 200 cases of diverticulum of the œsophagus have been studied and treated. The operative removal of the sac by multiple or single stage operation at the hands of various surgeons, which in the earlier days gave a mortality of 10 per cent, has, with improvements in technique, become very safe. Operative accidents, such as removal of an excess of œsophageal tissue, secondary stricture, the leaving of a portion of the sac with the resulting recurrence, injury of the recurrent nerve, œsophageal fistula, secondary hæmorrhage, and wound infection, have largely been eliminated by standardized methods. The need for a multiple stage operation which played an important part in the development of the operative treatment for diverticula has, with present technical improvements, largely disappeared.

A single stage operation may be done through a short, transverse incision without division of any important structure, with a period of disability lasting but a week or ten days, and without the necessity for secondary bougienage or further treatment. Primary union without infection of the wound is usual, the sac is removed with a precision and accuracy that is difficult to accomplish with a stage operation, and the scar is inconspicuous.

By the method of œsophagoscopic assistance devised by Dr. Jackson, the sac is quickly and positively located, during the operation leakage from the diverticulum or the sac is prevented, and a mandrin is provided upon which the opening in the hypopharynx or œsophagus may be accurately sutured without danger of constriction.

TECHNIQUE

Anæsthesia. The patient as a rule is partially narcotized by a retention enema containing avertin, or by the use of other narcotics. Rigidity of the jaws is undesirable. The field of operation in the neck is blocked and infiltrated in the conventional manner by freely injecting a 1 per cent solution of procaine containing suprarenin, 1:60,000. By blocking of the third and fourth cervical nerves at the cervical spines satisfactory analgesia may be obtained.

As a guide for the rapid introduction of the œsophagoscope into the subdiverticular orifice, a strong silk thread having three or four shot fastened at the end, is swallowed two or three days before the time of operation. The operation as a rule is not attempted until the shot are shown by roentgenogram to be in the ileum.

The transverse skin incision about 7 centimeters long and preferably in a wrinkle line, is carried from the midline of the neck at the level of the cricoid cartilage to about the middle of the left sternomastoid muscle. The skin, superficial fascia, and platysma are divided transversely; the few small vessels encountered are ligated by catgut. Small retractors are now introduced. The left pretracheal muscles and underlying thyroid gland with adjacent trachea and recurrent nerve are retracted medially, the common vascular sheath of the carotid and the sternomastoid muscle laterally. A sufficient exposure may be obtained without division of the superior thyroid artery or the omohyoid muscle. The middle layer of the deep cervical fascia is separated medial to the carotid artery thus exposing the longus colli and the left wall of the œsophagus. This part of the operation which is nearly bloodless, divides no important structures, and may be quickly and easily done.

While the wall of the œsophagus is thus exposed the diverticulum may be difficult to identify. To overcome this difficulty the œsophagoscope is now introduced into the sac, any contained liquid is aspirated and particles of food are removed with forceps. The sac is pushed up into the wound, where it gives off a deep red glow from

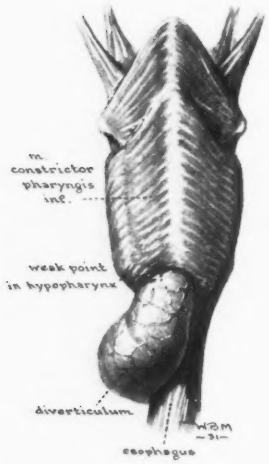

Fig. 1. The pulsion diverticulum of the œsophagus or more properly the hypopharynx, is a herniation largely of pharyngeal mucous membrane through the cricopharyngeous muscle, or the weak lozenge-shaped area above it. Originating posteriorly the sac usually passes down to the left of the œsophagus.

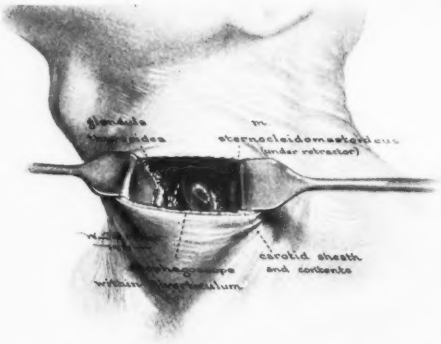

Fig. 2. Aided by an œsophagoscope introduced from the mouth into the sac the diverticulum is readily exposed through a short transverse incision on the left side of the neck at the level of the cricoid cartilage. It is not necessary to divide any important structure. The thyroid lobe is retracted medially and the sternomastoid muscle and carotid sheath laterally, while the omohyoid muscle lies medial and below the operative field.

the light in the end of the œsophagoscope. The sac is now grasped by soft viscera forceps and as the œsophagoscope is withdrawn into the pharynx the diverticulum which often is very thin and easily torn, is carefully separated from the surrounding tissues. The end of the swallowed thread having been drawn through the œsophagoscope, the instrument is now passed for a short distance down the œsophagus to serve as a guide in the removal of the sac and in the suture of the opening. The importance of this may be realized when it is understood that, in a number of instances sections of the œsophageal wall have been resected in mistake for the diverticulum.

After traction sutures of fine black silk have been placed at the upper and lower margins of the neck of the diverticulum the sac is accurately cut away by sharp, delicate (iris) scissors. With very fine curved eye or arterial needle the slit-like opening is very accurately closed with a continuous suture of very fine black silk, the finesse of an arterial suture being used. Great care is taken not to crush or traumatize the edges of the opening into the œsophagus and to make sure that the suture line is air- and watertight and that there is no laceration or residual opening into the œsophagus or hypopharynx. The mucous margins are wiped with small cotton swabs moistened with 3.5 per cent tincture of iodine and during the introduction of the suture the adjacent wound surfaces are protected with gauze moistened with 0.5 per cent hydrochloric acid in saline solution to prevent infection and stimulate early plastic adhesion. With constant aspiration through the œsophagoscope, there is no escape of liquid from the œsophagus.

The first row of sutures is now inverted by a row of interrupted sutures of very fine silk or silver wire (size No. 35). If the silver wire is used it is tied, not twisted, and the ends are cut short. The hair-like particles of the wire cause less irritation in a possibly contaminated field than other forms of suture material.

The tissues overlying the œsophagus are now further united by a third row consisting of interrupted sutures of fine silver wire or No. 000 chromic catgut. A very small split soft rubber tube drain (No. 10 to 12 F.) is introduced to the œsophagus below the line of suture. The platysma is united by interrupted sutures of No. 00 or 000 catgut, the skin by horse hair.

The special features of the operation are a short transverse incision leaving good support and an inconspicuous scar, the very limited exposure or separation of tissue in the wound, the avoidance of traumatism to the walls of the œsophagus, or any attempt to explore from the wound into the pharynx, and the very delicate but accurate watertight and airtight closure of the diverticular opening. For best results we believe that transfixion and ligation of the neck of the diverticulum should be avoided.

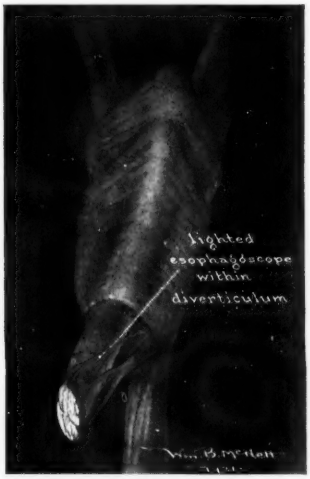

Fig. 3. From the light in the end of the Jackson œsophagoscope the diverticulum gives off a reddish glow in the depths of the wound, enabling it to be immediately recognized and grasped by forceps.

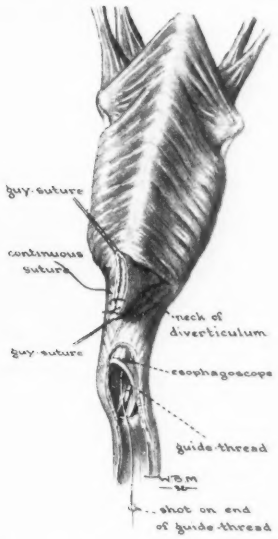

Fig. 4. The diverticulum having been isolated from the surrounding tissues the œsophagoscope, after aspirating the sac, is withdrawn and is guided by a previously swallowed thread into the œsophagus proper. The neck of the sac is divided and the slit-like opening in the hypopharynx very accurately closed by a continuous suture of fine black silk. Meanwhile the aspirating canal of the œsophagoscope keeps the field dry and free from pharyngeal secretion, and also prevents undue constriction of the œsophagus in suturing so that the later passage of bougies is unnecessary.

At the completion of the operation, the swallowed thread is cut and permitted to pass through the intestine. A small duodenal tube is carried through the œsophagoscope into the stomach and brought out through one nostril. The tube is fastened by adhesive plaster to the side of the face or forehead and is used for feeding during the first 7 to 9 days after operation. After being returned to bed, the patient is given a 2 liter enema containing 60 grams of glucose which, under the narcosis, is usually retained. Beginning 4 hours after the operation 60 cubic centimeters of 5 per cent dextrose solution is given through the duodenal tube every hour, provided there is no nausea. At the end of 24 hours 120 cubic centimeters of light liquid food is given through the tube every 2 hours. This amount is gradually increased and the interval lengthened until the patient receives 180 to 240 cubic centimeters of nourishing liquids every 4 hours. Care is taken to pass sterile water through the tube after each feeding, not only to cleanse the tube but to augment the patient's supply of fluid.

The small drain is removed at the end of 48 hours, unless there is local reaction. The swallowing of teaspoonful quantities of sterile water is tried after the sixth day. The duodenal tube is removed on the seventh to tenth day and thin liquids followed after 2 weeks by thicker liquids and very soft, semi-solid food such as thin gruels, junket, gelatin, and soft eggs. Solid foods, even if thoroughly masticated, are not permitted until at least 6 weeks have elapsed.

It is obvious that the operation should not be used unless a very accurate closure of the œsophagus without undue trauma or gross contamination of the wound is possible. Should infection or leakage from the pharynx into the wound occur, the wound should be freely opened, swabbed with tincture of iodine, and adequately drained. Thus far, however, in our experience we have had no serious complication arise from this type of operation.

FROM THE DIVISION OF SURGERY, THE MAYO CLINIC

TWO STAGE RESECTION FOR CARCINOMA OF THE RECTOSIGMOID AND RECTUM

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Division of Surgery, The Mayo Clinic

THE ideal operation for removal of carcinoma of the rectum and rectosigmoid has not been devised because a radical extirpative measure cannot be accomplished satisfactorily with preservation of the sphincteric apparatus. Furthermore, problems associated with carcinoma of the rectosigmoid are not always comparable to those which present themselves in cases of carcinoma of the rectum, and operative procedures aimed at removal of the one may not always be applicable to the other. The admirable prognosis in carcinoma of the rectum and rectosigmoid, compared with that of other carcinomata of the gastro-intestinal tract, counterbalanced although it is by an apparently unavoidable high mortality, urges continued efforts to reduce the death rate by improved technical maneuvers and standardized pre-operative and postoperative co-operative treatment by internist and surgeon. I do not believe that any one operation ever will be applicable to all types of carcinoma of the rectum and rectosigmoid, for the reason that the patients present themselves at such varying stages of the disease and, consequently, in different physical states, both as regards metastasis and local extension of the growth. However, it is my considered opinion that failure to apply radical extirpative procedures to a great many carcinomata in this situation is due largely to lack of courage, and that such failure withholds the just due of many patients whom mature judgment would indicate have ability to withstand such a procedure. The operation which rids patients of the growth, and at the same time avoids high hospital mortality, even though sacrifice of the splendid apparatus provided by nature is necessary, unquestionably will enhance favorably postoperative end-results.

There are several types of operation with which one must be familiar in dealing with rectal and rectosigmoidal carcinomata in order to cope advantageously with the various problems which present themselves at exploration. Of these types, I am convinced that a radical, combined, abdominoperineal operation in a single stage by which the local growth, and the gland-bearing tissue in immediate juxtaposition to it, are extirpated, after the fashion of Miles, or some modification which suits the individual surgeon's fancy, is the most desirable one. However, it has been impossible, in my experience, to apply this type of procedure in a single stage, as a routine, because of the high immediate mortality which follows its use. One should not reduce the horizon of operability too materially because of partisanship to a single maneuver and that, I think, is the most important consideration. Last year in the clinic, operability in cases of carcinoma of the rectum and sigmoid was 58 per cent, a very satisfactory operability no doubt, and one which may not be materially increased in the immediate future. Yet, in this 58 per cent of patients who were subjected to resection, less than one-third were judged proper risks for this type of operation. The patients who constituted risks graded 3 and 4 were treated by other types of maneuver.

To avoid the objections to many of the other proposed operative procedures and to preserve the desirable features of the single stage combined abdominoperineal procedure, it has been my custom recently to perform this operation in two stages. Colostomy and exploration are carried out at the first stage, the bowel being divided and the rectal end being dropped back into the peritoneal cavity, and the abdomen closed. A period of at least 6 weeks is allowed before the radical removal of the isolated segment is attempted. Removal is then accomplished by another combined maneuver. I have performed this operation in 23 consecutive cases with 1 death, an operative mortality of 4.3 per cent. With this encouragement, I hope to extend the selection of cases more widely, without unduly influencing the mortality, trusting that the end-results will be more satisfactory because of the radical type of procedure performed. This operation can be carried out with lower mortality in a larger group of cases than can the single stage operation, and just as wide dissection of the tissues is accomplished in the immediate vicinity of the growth. The operation avoids the undesirable blind loop which is left behind in operations of the Lockhart-Mummery or the Jones type. Likewise it permits the making of the most satisfactory type of colos-

tomy, a single-barreled one, through a small stab wound in the left flank. A colostomy of this type, in my experience, is much more readily controlled than is any other type and is much more easily made.

The acceptance of colostomy as a routine was one of the great steps forward in surgical treatment of carcinoma of the rectum and rectosigmoid, and yet, all procedures aimed at its performance leave something to be desired in the way of control. Satisfactory handling of colostomy is in direct proportion to the simplicity of its accomplishment; the simpler it is made, the more easily it is handled. Any simply performed colostomy, particularly if it is a single-barreled one, is easily controlled as long as the fæcal current is formed, and no colostomy yet devised is controllable or tolerable if the content of the bowel is liquid.

After the performance of the colostomy as the first stage of the combined abdominoperineal operation, the patients have returned home for a period of 6 weeks or longer, to gain weight and strength. They have returned for the resection in an infinitely superior physical state with the local infection around the growth markedly reduced by irrigations through a rectal tube. Another point to which I would call attention in this particular operation is its especial applicability to rectosigmoidal growths. I do not believe that carcinomata of the rectosigmoid can in any way be satisfactorily treated by colostomy and posterior resection of the growth at a subsequent stage. This, to my mind, constitutes local extirpation of the growth, which has numerous well known objections. The rectosigmoid, notoriously difficult of access, is the site of a great many carcinomata, probably of more than the ampullary portion of the rectum, and the nodal drainage therefrom, particularly that into the mesentery of the sigmoid, makes it necessary to remove more mesentery and adjacent tissue than is possible by a posterior type of excision. It is for growths in this situation, particularly, that the operation described is decidedly advantageous.

TECHNIQUE

In The Mayo Clinic, the diagnosis of carcinomata of the rectum and rectosigmoid, and as far up in the sigmoid as the juncture of the lower and middle thirds, is always made by proctoscopic examination and not by roentgenography. It is the custom, when a growth in this portion of the bowel is discovered, to take a specimen for biopsy with a cutting knife, and immediately with a cautery to touch the spot from which the specimen has been removed. Although numerous objections formerly have been raised to biopsy of malignant growths, I believe that proof of injury done, or of spread of carcinomatous cells by the method mentioned is totally lacking, and that the objection is based purely on opinion rather than on scientific conclusion. After adequate preoperative preparation of the patient, which aims mainly at decompression of the bowel by rectal irrigation, enemas, and judicious purgation, as well as at rehabilitation of the patient when that is indicated, exploration of the abdomen is carried out through a low median-line incision. Sistrunk called attention to the advantages of this incision, and with increasing use I have found it very desirable. Exploration is made in routine manner, from the superior portion of the abdomen down to the pelvis, the growth being touched last. Then, lightly and gingerly, the mobility of the growth and the chances of resecting it are determined. Beginning at the liver, as quickly as possible, the surgeon explores the surface of the two lobes for nodules, down the aorta, feeling the nodes around the pancreas and those on each side of the aorta, down into the bifurcation of the common iliac vessels and then down into the pelvis. Lastly, the growth is palpated, and if it is deemed resectable, a convenient portion of the

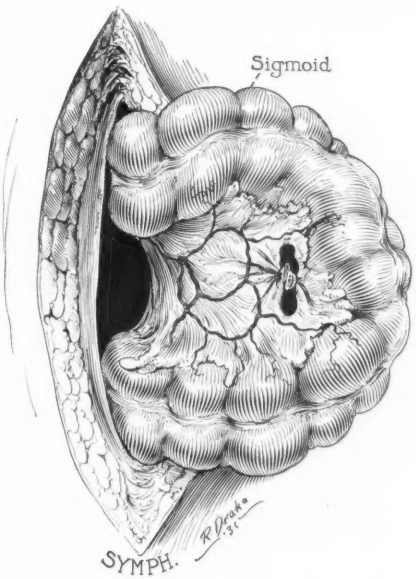

Fig. 1. Ligation of single vessel in mesentery of sigmoid close to the bowel.

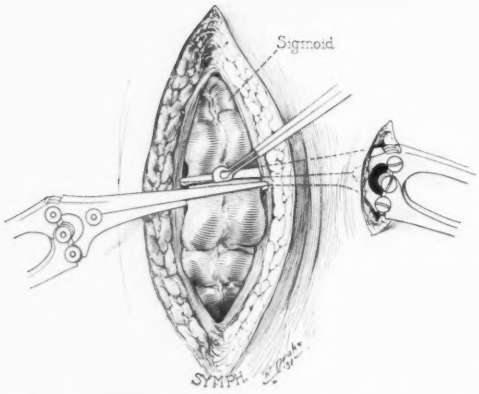

Fig. 2. Sigmoid divided between clamps. The proximal clamp is pushed through the stab wound in the left flank before being applied to the bowel.

sigmoid, that is, the highest point in the loop, is selected for the colostomy. The mesentery close to the bowel is divided (Fig. 1), and only sufficiently widely to permit the proximal end to be drawn out through a stab wound and the distal end to be dropped back. It is always possible to be sure of the blood supply to both ends, and any of the essential arteries are not divided. The superior hæmorrhoidal artery and its anastomosis with the necessary sigmoidal arches, are preserved under the eye. The rectal end of the bowel is turned in and the other end is brought out through a stab wound in the flank. To avoid false motion, it has been found desirable to make the stab wound in the flank as soon as the blood supply to the bowel has been tied off, and to push through this wound a Payr clamp which clasps the upper end of the bowel at the properly selected spot (Fig. 2). With another clamp approximated to this, but applied in opposite direction, the bowel is cut across and the proximal end is drawn out, while the distal end is turned in, as has been described (Fig. 3). The clamp obstructs the proximal end completely and is left on for 48 to 60 hours. Sutures are not put in the bowel to bind the peritoneum to it. In making the stab wound it is advantageous to cut down through the muscles of the abdominal wall. The incision is only about 5 centimeters long, and a smaller incision is made in the peritoneum, so that the peritoneum will hug the bowel closely. A piece of gauze going down to the peritoneum is wrapped around the end, the clamp is held on the abdomen by tape, after the median-line incision is closed, and is left, to be opened at the selected time (Fig. 4). Sutures

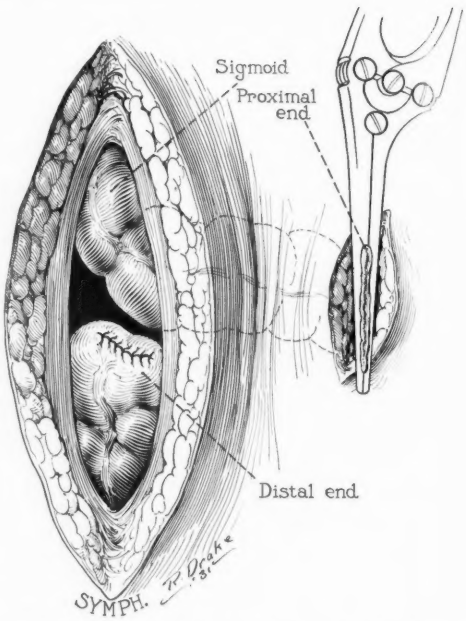

Fig. 3. After division of the bowel, the proximal end is drawn out of the stab wound in the flank and the attached clamp is left in place. The distal end is inverted and dropped back.

are not used in colostomy to attach the loop to the peritoneum or to any other layer of the abdominal wall. For a long time I have not attempted to assist nature in the healing process of joining peritoneum to peritoneum and do not regret omitting the sutures in this type of operation. The peritoneum is snug around the bowel and heals readily in 48 hours, or at most in 60 hours, and there is no disadvantageous small puncture into the bowel by a needle which may result either in leakage back into the peritoneal cavity and contamination, or in a small, annoying fistula beside the colostomy opening. It is questionable whether the mortality is higher in colostomy of this type than in the ordinary loop colostomy in which there is no manipulation. My mortality rate in ordinary colostomy is 3.5 per cent in operable cases and twice that high in cases which are considered inoperable, but in which nevertheless, exploration is performed. The clamp is taken off at the end of 60 hours or more, as is necessary. I have found it better to have the patient wait at least 6 weeks, and perhaps longer, before returning for the secondary resection. This, I believe, has been a distinctly important factor in

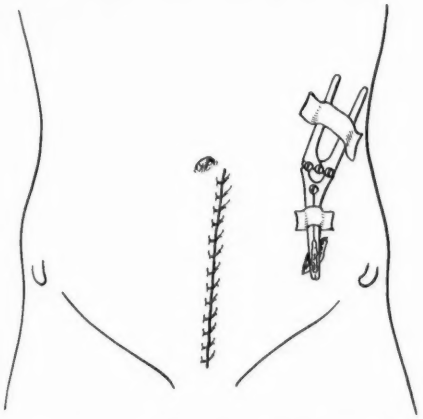

Fig. 4. Position of abdominal wounds and of clamp holding proximal portion of sigmoid.

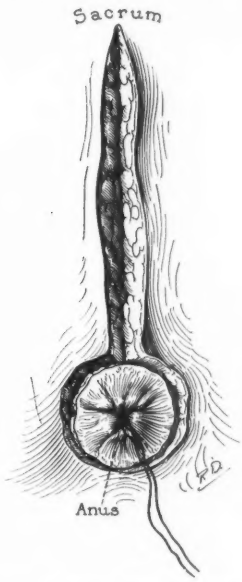

Fig. 5. Incision in skin over the sacrum and encircling the anus.

the successful accomplishment of this procedure. The objection is raised that the carcinoma may metastasize in this time, but I question if it is valid when this possibility is compared to the advantage of lowering operative mortality in a larger group of cases. When the patient returns, the resection is done, at first posteriorly, but finally by another abdominal incision.

This posterior type of attack and partial mobilization permits extensive dissection of the pelvis up to the peritoneum. Thus, it is possible to clean out the hollow of the sacrum and ischiorectal fossa, thus sacrificing the levator ani muscle and clearing away the gland-bearing tissues around the prostate gland and seminal vesicles in the male and from the posterior vaginal wall, cervix, and broad ligaments in the female. With the patient face downward on the table, with the hips elevated, and the anus closed with a pursestring suture, two concave incisions are made which extend from a little above the sacrococcygeal joint, around to the center of the perineum (Fig. 5). These incisions are carried downward, first on one side and then on the other, as much fat and gland-bearing tissue as is warranted being taken away down to the levator ani muscle, which is removed as high toward its bony attachment as possible (Fig. 6). I always sacrifice the coccyx but prefer to disarticulate it from the sacrum rather than to chisel off a piece of the sacrum, because this disarticulation is less likely to be followed by osteomyelitis and other unpleasant sequelæ. After the dissection has been carried out in this manner and the fascia propria has been divided opposite the sacrococcygeal articulation, the hand is thrust into the hollow of the sacrum and by blunt dissection all the tissues are separated from this bone. When the lateral dissection has been completed up to the peritoneum, but without its being opened, the entire rectum is encased in a rubber glove, which is tied tightly around the cuff (Fig. 7). The segment is dropped back into the hollow of the sacrum, and the posterior wound is closed. The patient is then turned on his back and the anterior part of the dissection is carried out. Through a low incision in the median line, the abdomen is opened and the pelvis is exposed and packed off from the remainder of the abdominal cavity, by wet gauze sponges. The peritoneum over the inferior mesenteric vessels is incised after identification of the left ureter (Fig. 8). This runs rather close to the vessels, but the right ureter is far distant and is never in danger of being ligated with them. When the peritoneum is opened over the vessels, they are hooked up over a finger, close to their origin, and doubly ligated and divided (Fig. 9). With the exception of the middle sacral artery, this is practically all of the blood supply to the rectum and sacral region, but the middle sacral artery, which is the terminal branch of the abdominal aorta, frequently will require a separate ligature. The peritoneum is incised forward, toward the base of the

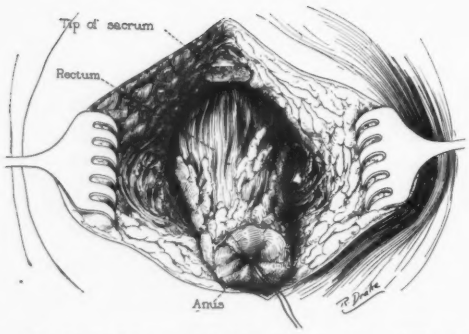

Fig. 6. Excision extended showing partial mobilization of rectum. Coccyx removed.

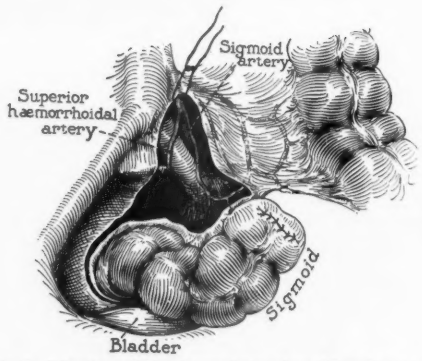

Fig. 8. Ligation of blood supply to sigmoid and rectum.

bladder on both sides, and the bladder is separated from the rectum. The gland-bearing tissue is wiped mesially from both sides with gauze, and the entire segment is lifted out through the abdomen (Fig. 10). The large cavity thus opened must necessarily heal by granulation tissue, and no attempt is made to close it without drainage. After peritonization of the pelvis, that is, after making a new pelvic floor, the abdomen is quickly closed. I have never had much difficulty in peritonizing the pelvis. If the patient is a woman there is no difficulty because of the utilizable broad ligaments and the uterus; if a male, there is almost as little trouble, if one uses the peritoneum over the bladder and mobilizes the lateral portion of the peritoneum satisfactorily.

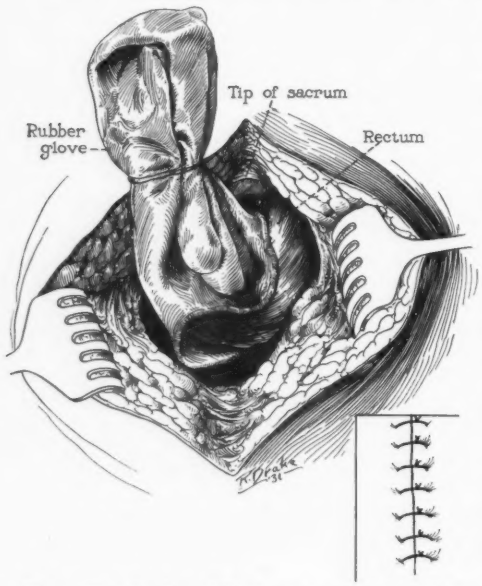

Fig. 7. Completely mobilized rectum encased in rubber glove. Insert shows wound closed after segment is dropped back in hollow of sacrum.

The abdominal part of the operation may be accomplished quickly, and is bloodless after ligation of the inferior mesenteric vessels. After the wound is closed, two of the lower sutures in the posterior wound are removed, and a small gauze pack is put into the hollow of the sacrum for drainage. The entire second stage of the operation is neither difficult nor time-consuming, and utilizes the most satisfactory principles of the radical procedure, with lowering of the primary mortality as it is done in two stages instead of one.

The postoperative convalescence in my cases has been similar to that in cases in which posterior resection has followed colostomy, and usually the wound has healed completely in about 3 months. Sometimes it takes longer but when once healed, there is no disadvantageous, irritating, and undesirable mucous fistula from a blind loop. A single-barreled, satisfactory colostomy is established, and the radical type of attack on carcinomata in this situation has been carried out.

I would emphasize that the preliminary preparation of these patients, the proper decompression of the colon whenever it is possible without a drainage procedure, and the permitting of long periods to elapse between stages, seem to me to be the most valuable adjuncts toward the success of any radical, graded procedure. That there are disadvantages must be admitted, for any operation whereby the abdomen must be invaded twice within a period of a few months is not free from an opening for criticism. Yet, if satisfactory operative mortality can be maintained, without

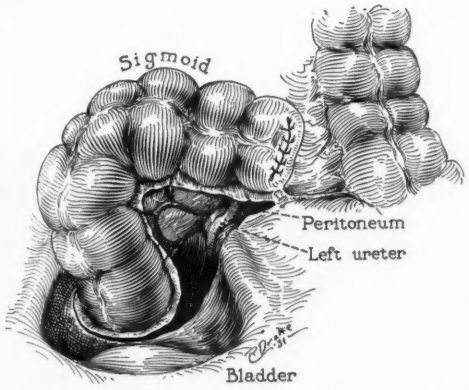

Fig. 9. Division of peritoneum for mobilization of sigmoid and exposure of left ureter.

the sacrifice of any steps which should increase, rather than diminish, the horizon of operability, I believe the procedure merits consideration and trial.

Appended is an epitome of the case which terminated fatally in this series of 23 consecutive cases. In the series there were only 5 cases which I deemed of sufficient gravity, from one standpoint or another, to justify refusal of this radical type of operation, and in which colostomy and subsequent posterior resection were performed. This confirms the assertion, I believe, that with increasing use one finds a wider scope for the more radical type of removal.

A man, aged 69 years, whose past history was essentially negative, was admitted to the clinic with a history of rectal bleeding and diarrhœa that dated from a hæmorrhoidectomy 10 months previously. Also dating from this operation was evidence of diabetes mellitus which, on the patient's admission to the clinic, was satisfactorily controlled by diet. The patient appeared to be in a state of general debility. He had lost 15 pounds in weight and laboratory examination disclosed evidence of moderate secondary anæmia. Marked general arteriosclerosis, myocardial degeneration, and mitral insufficiency (compensated) were noted. The prostate gland was moderately enlarged, and mild urinary symptoms were present. Proctoscopic examination disclosed adenocarcinoma graded 2 of the rectosigmoid; the growth was fixed posteriorly and was causing moderate obstruction.

After a period of hospitalization, during which rehabilitation measures were instituted and intraperitoneal vaccine was administered, exploration was carried out under spinal anæsthesia. Metastasis could not be made out.

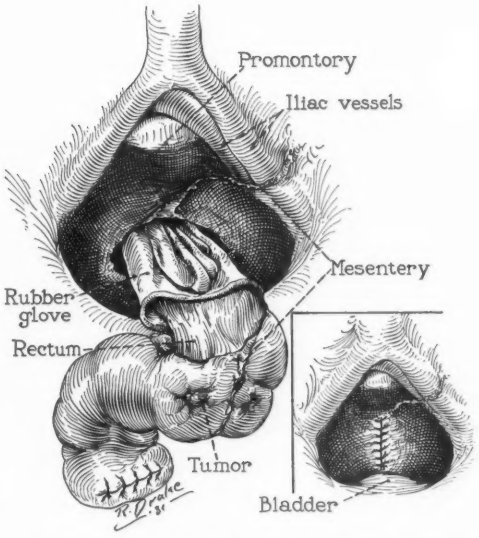

Fig. 10. Anterior approach. Entire rectum being lifted out of hollow of sacrum. Peritonization of pelvis completed.

The sigmoid was found to be diffusely studded with diverticula and a little above the rectosigmoid juncture was a large tumefaction. A single-barreled colostomy was performed as the first stage of abdominoperineal resection of the rectum. Within 24 hours there were signs of impending diabetic coma which required the administration of large doses of insulin. Aside from this complication, the patient recovered satisfactorily and after 5 weeks was able to control the diabetes by diet alone. Three months at home brought about general improvement in his condition. In spite of the grave risk which further operation would entail, the patient and his relatives were insistent that the rectal growth be removed. Following its removal as the second stage of combined abdominoperineal operation and until the patient's death, 70 hours later, the total urinary output was only 460 cubic centimeters. Signs of uræmia appeared early and became progressively more intense. There was no evidence of peritonitis.

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FURTHER OBSERVATIONS ON THE USE OF CASTOR OIL, QUININE, AND PITUITARY EXTRACT IN THE INDUCTION OF LABOR

An Analysis Based on the Study of Three Hundred and Twenty Consecutive Cases from Private Practice[1]

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IN February, 1927, in the *American Journal of Obstetrics and Gynecology*, one of us (Mathieu) reported observations on 91 cases in which castor oil, quinine, and pituitary extract were used for the purpose of inducing labor. At that time it was stated:

"Much of the advantage of prenatal care is lost if one allows the head of the fetus, by sheer growth, to reach a stage of marked disproportion with the pelvis of the mother who carries it, when induction might have avoided this complication.

"Women with histories of rapid or precipitate labors, or with thin, dilated cervices at term, should not be allowed to suffer precipitate labor while on the way to the hospital. Nor should those with toxæmia, progressive, in spite of treatment, be further endangered by delay. The woman at term who is suffering distress and discomfort due to pain, pressure, insomnia, and nervous anxiety, should not be permitted to reach the stage of exhaustion because one wishes to let Nature take her course. Nor is it good obstetrics to allow a woman near term, whose membranes are ruptured, to go longer than 24 hours without inducing labor."

In that paper was described a modification of the dosage used in the method of Watson whereby the main objectionable feature of the Watson method was overcome by reducing the dose of pituitary extract to 3 minims for each injection. Among other data, this series of carefully analyzed cases revealed the following facts: There were 3 failures, a percentage of 3.3; the morbidity among the mothers was 4.4 per cent; there were no harmful effects seen from the use of these drugs in induction and there were recorded no maternal or fetal deaths, either early or late.

The present paper has to do with an analysis of 320 consecutive induction cases, all taken from the private practice of one of us (Mathieu), and includes all the patients in whom labor was induced during the 9 years from 1922 to December, 1930. In the entire series, there were 153 primiparæ and 167 multiparæ. All of the patients were of the white race.

INDICATIONS

The indications for induction were as follows:

	Cases
Postmaturity	62
Postmaturity with	
Large baby	31
Premature rupture of membranes	13
Distress and discomfort	12
Fear of precipitate labor	5
Multiple fibroids	1
Maturity with	
Large baby	43
Distress and discomfort	36
Contracted pelvic outlet	19
False pains	16
Fear of precipitate labor	4
Former dead baby	3
Prematurity with	
Toxæmia of pregnancy	34
Premature rupture of membranes	16
Breech presentation	7
Death of fetus before onset of labor	5
Contracted pelvic outlet	4
Eclampsia	3
Chronic pulmonary tuberculosis	3
Placenta prævia	2
Bilateral pyelitis	1

METHOD

The method used is practically identical with the one presented in the early report, 3 minims of pituitary extract being used at each injection.

The method is as follows: In the hospital, the patient is given 2 ounces of castor oil and 10 grains of quinine sulphate and exactly 2 hours afterward, a hot soapsuds enema. As the enema is about to be expelled, 3 minims of pituitary extract are given hypodermically. This same dose of pituitary extract is repeated every 30 minutes until labor starts and *no longer*. From then on, the labor is conducted as though the onset has been normal. Failure is admitted and the procedure stopped if 8 hours pass without labor being started or if there is absolutely no sign of any effect toward induction or if the continued use of the injections is too trying to the mother. In such cases the procedure is stopped, the mother is given an hypnotic or sedative and after 24 or 48 hours, the induction is again attempted.

[1]Read before the Portland Society of Obstetricians and Gynecologists, December 16, 1930.

Over 2 years ago, the quinine sulphate dosage was cut from 10 grains to 5 grains. The last 120 inductions were made without any quinine sulphate whatever. We feel that the induction can be done without the quinine; and since several authors have reported intra-uterine deaths which they think were caused by quinine, we feel that it is better to do without it.

All of the inductions have been done by two nurses who are highly specialized in these matters. The method is as follows: Two ounces of castor oil is given early in the morning, preferably at 6 o'clock; exactly 2 hours later a hot soapsuds enema is given. In certain cases labor will commence at this stage and it is unnecessary to proceed further. In the majority of cases, however, as the enema is being expelled 3 minims of pituitary extract is given hypodermically; this is repeated every half hour until labor commences or until 15 injections have been given without effect. During the entire induction the gravida should be flat on her back with only one pillow for the head; failures might follow if she is allowed to walk about. In the event of failure, a sedative is given and stimulation is started again within 24 or 48 hours, with the same routine. *The injections are stopped as soon as labor begins.* Nasal stimulation, with one cubic centimeter of pituitary extract on cotton applied to the mucous membrane of the nose, has been used instead of the hypodermic injections.

Thirty-nine cases (12.2 per cent) in this series were successfully induced with castor oil, quinine, and the hot enema. The remainder necessitated hypodermic administration of pituitary extract. In 4 cases induction with nasal applications of pituitary extract, using the method of Hofbauer, was successful. In four cases thymophysin was used. We feel that thymophysin has the same action as pituitary extract and notwithstanding many published reports, we feel that it has added nothing to our armamentarium. Incidentally, we have used thymophysin for inertia in the second stage of labor after having read the reports of Jarcho and others. We have learned from clinical experience what Rucker found with the bag and manometer, namely, that thymophysin does not act differently than pituitary extract and that the same contra-indications should prevail against its use as prevail against the use of pituitary extract.

SUCCESSES

There were 309 successful inductions (96.6 per cent) in the series. The following analysis shows the number of attempts at induction necessary before success was attained.

Number of attempts	Cases
One	216
Two	62
Three	24
Four	4
Five	3

A word of explanation seems necessary regarding those cases in which several trials at induction were made before the induction was successful. We have always been extremely careful in trying to make the induction safe, particularly in an effort to avoid an injection of pituitary extract after labor had apparently started. In not a few cases we have purposely stopped the injections when there was any uncertainty as to whether or not the patient was actually in labor—accepting a failure rather than assuming a risk.

Consider the nervous and anxious patient in the last fortnight of her pregnancy, whose uterus seems to be on the verge of evacuating its contents. Every evening in this period when the clothes are removed, contractions of the uterus start and continue in the regular manner for several hours, ceasing when the patient falls asleep. We cannot state whether this is a nervous phenomenon or whether it is actually a forerunner of true labor, but we know from clinical experience that this type of patient presents the most difficulties. During the induction regular contractions of the uterus start after a few injections of pituitary extract only to stop entirely several hours after the administration has been stopped. As previously stated, this type of patient has given us the most trouble. In our attempts to be absolutely safe we have preferred discontinuing the attempted induction, giving the patient a sedative and a good night's sleep, and renewing the attempt on the following day.

The average number of injections for 145 primiparæ, in all of whom the induction was successful, was 6.7. Four of these cases had nasal applications of pituitary extract by the method of Hofbauer. When nasal applications of pituitary extract were used, there were no hypodermic injections given.

The average number of injections for 164 multiparæ, in whom the inductions were successful, was 6.0. Of the failures in the series that were later followed by successes the average number of injections given the primiparæ were 11.4 and the multiparæ 9.1.

The highest number of injections necessary to insure success in a primipara was 16 and in a multipara 14; the lowest number given in the failures was 3 in a primipara and 4 in a multipara. The average length of labor of the successful

primiparæ was 11.1 hours. The 2 longest labors were 92.5 and 52 hours. In these 2 longest labors, the real length of the labor is indefinite because in the first half of the labors, the uterine contractions were more or less irregular with lapses of some hours without contractions. The shortest labor was 1 hour and 45 minutes. The average length of labor in the successful multiparæ was 4.5 hours. The longest labor was 17 hours and the shortest 45 minutes.

With the head deeply engaged, the cervix effaced, and the external os admitting a finger, the chances of a successful induction were greater than in those cases in which the head was floating and the cervix was not effaced. This was noted alike in primiparæ and multiparæ. In many cases necessitating several trials at induction, the head was floating at the first attempt; by the second or third attempt, the head had become deeply engaged and success was easily obtained. With both engagement and effacement present, the number of hypodermic injections necessary to induce labor was lessened and the total length of labor was slightly shortened.

In the 29 cases of spontaneous premature rupture of the membranes, and in a few others in which the membranes were ruptured artificially because of some urgency, the induction was one hundred per cent effective on the first trial. We hope it will be noted that in the entire series of three hundred and twenty attempted inductions, there was not one single case of prolapse of the cord, the one serious objection to induction by bag or bougie.

The following tabulations illustrate facts:

	Vertex engaged or partially engaged	Not engaged
Successes	230	70
Failures	6	5
Hours of labor	7.5	9.8
Number of hypodermic injections		
Unsuccessful trials	9.5	12.1
Successful trials	4.0	5.8
Breech presentation—6 cases.	Not specified—3 cases.	

	Cervix effaced	Cervix not effaced
Successes	237	68
Failures	5	6
Hours of labor	7.7	13.1
Number of hypodermic injections		
Unsuccessful trials	10.6	10.4
Successful trials	4.4	8.0
	Not specified—4 cases	

The average weight of the living babies was 3,558 grams. Ninety-four babies weighed over 3,800 grams and 5 weighed under 2,200 grams. The 2 largest babies weighed, 4,810 and 5,586 grams; the 2 smallest, 1,370 and 1,345 grams.

There were eleven failures following attempts at induction with castor oil, quinine, and pituitary extract.[1]

MORBIDITY

There were 23 cases of morbidity (patients who had a rise of temperature up to 100.4 degrees on two different days excluding the day of delivery), 7.2 per cent for the entire series. In no case did it appear that the morbidity was directly due to the induction of labor. The following table shows the cause of the morbidity:

Cause of morbidity	Cases
Pyelitis	6
Infected perineum	5
Mastitis	5
Phlebitis	3
Pleurisy	1
Pneumonia	1
Infected pubiotomy wound	1
Hæmorrhage, postpartum	1

MORTALITY

There were no maternal deaths. There were no fetal deaths directly due to the method of induction. There were 9 fetal deaths in the series; 5 of which were macerated fetuses, dead before the induction was started and the inductions were done because it was obvious the babies were dead. There were 2 stillbirths. One of these babies died *in utero* during an eclamptic convulsion of the mother who had no prenatal care and who was an emergency case; the other died from strangulation of the cord just prior to delivery due to a short cord wrapped tightly twice about the baby's neck. There were 2 neo-natal deaths, both due to congenital anomalies.

CLASSIFICATION OF FETAL DEATHS

	Cases
Macerated fetuses at term	
Toxæmia	2
True knot in cord	1
Macerated fetus at 8 months (toxæmia)	1
Macerated fetus at 5½ months (mother had multiple uterine fibroids)	1
Stillbirths	
Died during eclamptic convulsion	1
Strangulation of cord	1
Neonatal deaths	
Died fourth day—congenital occlusion of bile ducts and patent foramen ovale	1
Died twelfth day—hydrocephalus	1

	Per cent
Total fetal mortality	2.8
Stillbirth mortality, including macerated fetuses	2.2
Neonatal mortality	0.6
Corrected total fetal mortality, eliminating macerated fetuses and deaths due to congenital defects	0.6

[1] The details of the failures will be found in the reprints.

METHOD OF DELIVERY

The method of delivery following induction was as follows:

Type of delivery	Cases
Forceps delivery	
Mid-forceps	65
Low-forceps	119
Control-forceps	63
Total	247
Spontaneous delivery	49
Version and breech extraction	12
Breech extraction	7
Cæsarean section	1
Mid-forceps and pubiotomy	1
Twin delivery	3
Mid-forceps	2
Low-forceps	3
Breech extraction	1

SUMMARY AND CONCLUSIONS

1. In a series of 320 cases in private practice, the castor oil, quinine, and pituitary extract method of induction of labor was successful in 96.6 per cent of the cases.

2. Induction caused no increase in the maternal mortality, the maternal morbidity, fetal mortality, or fetal morbidity.

3. Induction was most successful when the head was engaged and the cervix effaced.

4. Induction was apparently not responsible for the occurrence of any pathological conditions during labor, delivery, or the puerperium.

5. In the last 120 inductions, quinine was not used and the results were apparently not affected by its omission.

In this series of 320 cases, there appeared no basis for the fear some hold that the use of pituitary extract in the induction of labor causes separation of the placenta.

In this number of cases, which on close analysis seem to include most of those cases that promise trouble (the toxæmias, eclampsias, large babies, contracted pelvic outlets, etc.), the maternal morbidity and the fetal mortality were surprisingly low; in fact, it appears to us that in this series the induction saved much maternal morbidity and several fetal lives.

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THE ROENTGEN-RAYS AND RADIUM IN THE DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE BLADDER[1]

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THE injection of air into the bladder for the demonstration of tumors has been used by me for diagnosis and for teaching since 1910 and the technique was discussed by me at various meetings of roentgenologists. Realizing that this procedure was not in general use, I presented a formal paper upon this subject before the Philadelphia Roentgen Society on May 8, 1919. Since then this method has been used more and more but even now is, I believe, much neglected. This modified roentgen method of examining the bladder has not been routinely used in the past, evidently because of the great skill that has been developed by the expert cystoscopist. In my opinion, additional information will be obtained in most cases, if a pneumocystographic study is combined with the cystoscopic examination, but there are many cases in which a satisfactory cystoscopic examination is not practical for the following reasons: (1) because of the severe pain which generally accompanies these cystoscopic examinations, unless under a general anæsthetic; (2) because of inability to pass the cystoscope; (3) because of severe hæmorrhage which clouds the field; (4) because of decided objection on the part of the patient; (5) because an expert cystoscopist may not be at hand.

TECHNIQUE FOR PNEUMOCYSTOGRAMS

It is my custom to make an anterior and a posterior film of the bladder region before any air is injected. This preliminary film will demonstrate any opaque calculus that may be present, and will particularly demonstrate any localized collection of gas in the rectum or colon which may be confusing in the interpretation of the subsequent pneumocystograms. The urethral orifice is then cleansed and all of the usual precautions and preparations are made which are necessary for passing a soft rubber catheter. A sterile soft rubber catheter of the largest size that will pass without pain or inconvenience is then introduced. If there is an obstruction from a prominent middle lobe of the prostate, one may use a prostatic catheter. Any residual urine should be withdrawn, for a soft tumor surrounded by fluid may not be demonstrated. Occasionally one does not succeed in removing all of the urine, but if air is injected and one *examines the patient anteriorly and posteriorly* there will be one of these two positions in which the tumor will be surrounded by air, as I shall demonstrate to you (Figs. 1, 2, and 3).

After the urine has been withdrawn, an atomizer bulb is attached to the catheter by means of a tapering glass connecting rod, and then by gentle compression with the thumb and index finger air is pumped into the bladder until the patient complains of bladder distention or until one can feel the distention of the bladder by palpation or outline it by percussion. A pair of hæmostatic forceps is clamped upon the catheter and both of these are strapped to the thigh by means of adhesive plaster, all of which is prepared in advance so as to minimize the delay and distress from bladder distention. To economize time, all of these procedures are taken with the patient on the Potter-Bucky diaphragm with tube and film in position so as to make the exposures with the least possible delay.

If the injections are made slowly and due attention is paid to the patient's complaint of pressure, I believe, no harm can result. I know of no instance of an air embolism developing, and can see no reason for it since pneumopyelography has been used with success. Surely, if the kidney pelves can be distended, with air, one need not fear the distention of the bladder.

One or more 8 inch by 10 inch films are made posteriorly, directing the rays in line with the axis of the pelvis, and then one or more films are made anteriorly, the patient being carefully turned upon the abdomen and the rays directed obliquely, anteriorly, and upward, I usually make several films with some variation in the exposure in each position.

Generally, *the anterior view will give most information*, but both views are essential. After the examination has been finished the patient is turned to the supine position and by the release of the clamp the air is quickly expelled. A little pressure over the bladder will be helpful. If by chance the catheter comes out of the bladder, a sterile one should be inserted and the air allowed to escape. It is generally advisable to compress the bladder to expel all of the air.

After several hundred such examinations, I have not had any serious objection on the part of

[1]Presented by invitation before the Philadelphia Urological Society, January 26, 1931.

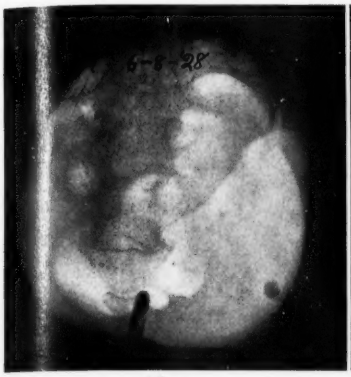

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. No evidence of the bladder tumor was noticeable June 8, 1928, because it was surrounded by 8 ounces of fluid, which we did not succeed in removing preceding the pneumocystogram, made with a posterior film. Case 1.

Fig. 2. We then turned the patient in the prone position and this pneumocystogram *shows very clearly the two tumors of the bladder.* The large one from which the specimen had been removed and the other smaller one, indicated by arrows, June 8, 1928.

Fig. 3. Another anterior film made in the prone position *shows complete disappearance of the tumor* May 8, 1929, and the patient has remained free from symptoms and has been found free from disease also cystoscopically by Dr. Haines. Briefly, the history is as follows:

Mr. A. T. G. T., aged 49 years, was referred on May 21, 1925, by Dr. Francis J. Dever of Bethlehem, Pa., on account of leucoplakia involving the glans penis. This was found later to be carcinoma, and was treated by electrocoagulation and radium applications, with temporary cure. A recurrence, however, developed and on June 2, 1930, I removed the glans penis and sulcus completely by electrocoagulation, with no evidence of recurrence and complete comfort and freedom to date.

On June 8, 1928, he returned to us with the history of hæmorrhage from the bladder, and cystoscopic examination by Dr. Wilbur Haines showed evidence of carcinoma within the bladder. We then obtained the history that he had been sent to Dr. Estes of Bethlehem, 3 years previously on account of bleeding from the bladder. On June 8, 1928, Dr. Haines found a tumor about the size of an English walnut, and removed a specimen for microscopical examination. This was reported by Dr. Eugene Case as papillary carcinoma of the bladder. Dr. Haines did two subsequent destructions on this tumor mass, and he received from us the following X-ray treatment.

He was given high voltage X-ray treatment through four fields, 2 anteriorly and 2 posteriorly, crossfiring upon the bladder giving a 100 per cent through each area, between June 15 and July 10. He has had a second course of precautionary treatment, and re-examination of the bladder by pneumocystogram on May 8, 1929, which showed the tumor entirely gone.

the patient and no damaging effect. One patient developed a chill shortly after this examination, from which he promptly recovered, but it is well known that a chill may occasionally follow any catheterization.

TUMORS DEMONSTRATED

By this means I have succeeded in demonstrating several hundred bladder tumors, and so far as I know have failed to demonstrate only one. Tumors of the size of a thimble to a size that fills the entire bladder have been shown. They have been demonstrated in all parts of the bladder. One can demonstrate the size, position, outline, and *degree of infiltration.* One really demonstrates not only the filling defect, but the flexibility or lack of distensibility of the bladder wall. The serious sign of malignant disease is *infiltration* and the part of the bladder wall which is infiltrated by a malignant growth cannot be distended. This gives information which I believe

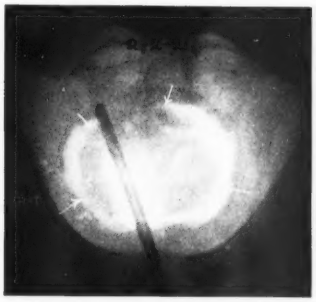

Fig. 4. Showing tumor mass size of a goose egg. Mr. D. S., aged 55 years, referred by Dr. W. Mackinney, February 2, 1921; frequent voiding of bloody urine for 1 year. Tumor mass destroyed by electrocoagulation through a suprapubic cystotomy by Dr. Mackinney and myself, and 13-10 milligram radium needles introduced into base of tumor for 8 hours, half anteriorly and half posteriorly, making 150 per cent in tumor area during a period of 4 months. He lived 9 years, and died October, 1930, of intercurrent disease. Case 2.

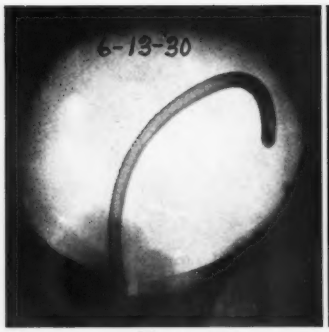

Fig. 5.

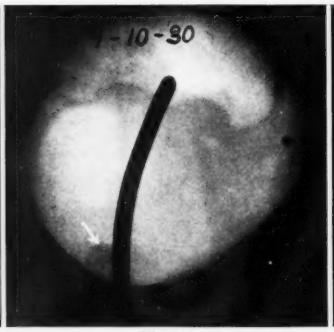

Fig. 6.

Fig. 7.

Fig. 5. Case 3. Shows the tumor mass with a base approximately 5 centimeters in diameter, June 13, 1930, surrounding the neck of the bladder.

Fig. 6. This tumor mass was reduced to about one-sixth its original size by September 10, 1930.

Fig. 7. Tumor has completely disappeared January 16, 1931, and the patient is free from all symptoms. Briefly, the history is as follows: Mrs. G. W. S., aged 55 years, referred by Dr. James M. Anders, June 13, 1930, used to illustrate the complete disappearance of the broad based irregular nodular tumor about the neck of the bladder which showed progressive reduction and disappearance under X-ray treatment, given with high voltage X-rays (200 kilovolts, 2 millimeter copper filter, at 40 centimeter distance), through three fields of treatment, one anteriorly, and two through the sacrosciatic notches directed into the tumor area giving approximately 250 per cent of an erythema dose through each portal. In addition to the X-ray treatment given as above indicated, the patient had on November, 17, 1930, in the form of a radium pack, inserted into the vagina, 100 milligrams of radium filtered through 2 millimeters of platinum, at a distance of 2 centimeters directed toward the tumor from posteriorly, the rectum being protected, for a period of 24 hours.

cannot be obtained otherwise without operation and will be useful in determining the method of treatment to be chosen.

One cannot always decide by pneumocystography whether a growth is malignant or not, but if the tumor is large, with a broad infiltrating base, and occurs in a patient past the age of 35 years one can be reasonably certain of the tumor being malignant. If the tumor is small in size, or multiple, pedunculated, and not infiltrating (bladder distending smoothly and evenly in all directions) then we may assume that it is benign. A cystoscopic biopsy is necessary to make an exact diagnosis but this is subject to error and depends upon the portion of the tumor taken. Pneumocystography is in no sense intended to replace cystoscopy.

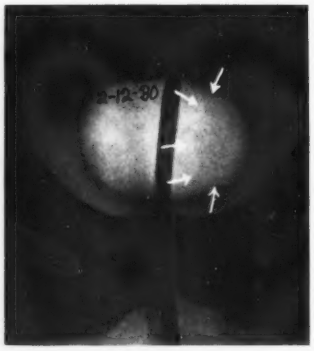

Fig. 8. The shadow of the tumor mass is seen in the posterior film made in supine posture. The shadow is less clear because some urine partly obliterates part of it.

All growths of the bladder are potentially malignant, and should be removed, either by destruction, by electrocoagulation, by the thermocautery, by excision, by radium applications, by means of roentgentherapy, or by some combination of these methods. In all cases the disease should be recognized as early as possible and treated thoroughly from the beginning. This simple procedure will be useful in recognizing early carcinoma, but cannot be depended upon as final in the elimination of early carcinoma or of a small tumor in the bladder.

IRRADIATION TREATMENT

Irradiation may be applied in various ways but no methods have yet produced enough cures to make us enthusiastic, nor to make us feel satisfied. This dissatisfaction also applies to surgical excision. The dissatisfaction from surgery is indicated by such records as that of Lower who reports a series of 222 cases of bladder tumors of which 108 were malignant; 81 of these malignant cases were operated upon with an operative mortality of 9.8 per cent, and a death rate within a

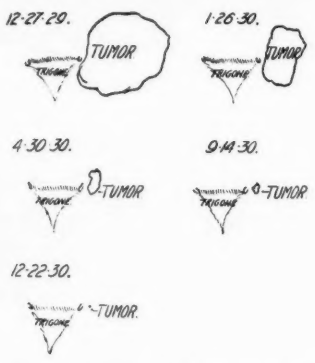

Fig. 9. Various diagrams made by Dr. McCrae on the dates as indicated in the illustration.

Fig. 10. Complete disappearance of the tumor with a perfectly normal distention of the bladder wall, as a result of the irradiation treatment, no other treatment having been given. Briefly the history is as follows: Mr. H. C. T., treated by Dr. E. Spackman, was under my direction since January 6, 1930. Patient had been passing bloody urine during 5 or 6 months. Cystoscopic examination made by Dr. Lowraine McCrae and pneumocystogram by us showed an infiltrating carcinoma about the size of a half dollar, occupying the bladder in the region of the left ureter. The patient received treatment through one portal of entry anteriorly, a total of 325 per cent, and 400 per cent of an erythema dose through each sacrosciatic notch, by means of high voltage X-rays (200 kilovolts, ½ millimeter of copper filtration, 50 centimeter distance), this giving approximately 400 per cent in the bladder area.

year after operation of 51 per cent, and only 7 per cent were 5 year cures. Scholl reports that in 168 operative cases, 36.6 per cent with malignant papillomata died within a year, and 71 per cent with solid tumors died within an average of 7½ months, and that the operative mortality in papillary carcinoma was 12 per cent and with infiltrating carcinoma 20 per cent. *It must not be forgotten that these results have been obtained in "operable" cases, while irradiation is used almost entirely in "inoperable" cases*, except by Barringer, who uses operation for the placement of radium. The radiation methods may be any of the following:

1. Unscreened radium may be applied directly in small tumors and tumors about the neck of the bladder, the radium being held in direct contact through a cystoscope as recommended by Barringer.

2. Seeds either of glass or, better, gold may be implanted directly into the base of the tumor, cystoscopically or suprapubically as recommended by Barringer, Keyes, Hyman, Burnam, Marson, and others, but is suitable only for small tumors.

3. The disease may be excised and then treated by deep roentgentherapy.

4. The disease may be destroyed by electrocoagulation and then treated by the implantation of removable radium needles as has been used by us for a time, only in very large and inoperable tumors, through a suprapubic cystotomy but which method has now been abandoned by us (Thomas and Pfahler, MacKenzie, and others).

5. Through a suprapubic cystotomy the prominent tumor may be snared away and the base implanted with radium seeds (Barringer).

6. Deep roentgentherapy may be used upon the primary tumor as has been recommended by Waters, Gunsett, Schmitz, Schnoebelin, and others, and which method seems to me to be most satisfactory. It is to be recommended especially in the inoperable tumors, and preliminary to operation. Inoperable tumors are those in which operation is contra-indicated because of the poor general condition of the patient; by the size or location; or because of absolute refusal on the part of the patient. (Barringer classifies as inoperable: (a) multiple carcinomata or large carcinomata of a base more than 4 centimeters in diameter, (b) carcinomata which have affected the trigone and posterior urethra, (c) carcinomata which have been previously operated upon and have recurred, (d) carcinomata in patients whose age or condition contra-indicated shock of operable removal.)

7. The tumor may be destroyed by electrocoagulation and then highly filtered radium (equivalent of 4 millimeters of lead) capsules packed into the bladder against the base of the tumor. This method appeals to me strongly and at some later date will be reported in detail.

George G. Smith finds about the same end-results from excision, electrocoagulation, and radium treatments, 27, 27, and 29 per cent respectively, free from symptoms after 2 years.

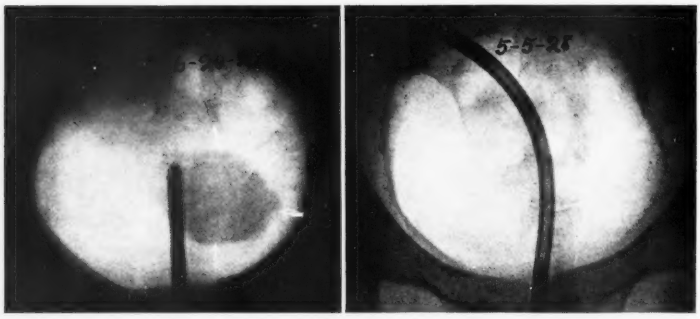

Fig. 11, left. Case 5. Mrs. E. K., aged 59 years, referred by Dr. H. J. Tumen. Patient was injured by a fall November 15, 1926. On the day following, she passed bloody urine. She noted bloody urine repeatedly and first saw Dr. Tumen May 31, 1927. A cystoscopic examination made by Dr. John B. Lownes showed a tumor mass in the region of the left ureter, the size of a lemon. He recommended X-ray or radium therapy instead of operation. On June 20, 1927, pneumocystogram showed an irregular broad-based tumor mass approximately 4 centimeters in diameter, overlying the region of the left ureter. She was given high voltage X-ray treatment directed through a field anteriorly, and over the tumor area anteriorly, and through each sciatic region, crossfiring upon the tumor area giving 200 per cent of an erythema dose over each of these areas which would equal approximately 200 per cent of high voltage X-rays, filtered through ½ millimeter of copper which gives approximately 200 per cent in the tumor area. This treatment was all given within a period of about 5 weeks, resulting in the complete disappearance of the tumor.

Fig. 12. Shows a pneumocystogram made May 5, 1928, showing complete disappearance of the tumor area from high voltage X-ray treatment alone, and this was confirmed by studies made by both Dr. Tumen and Dr. Lownes. She has had no symptoms since.

Barringer is more enthusiastic. In 98 cases with a pathological diagnosis, there were 43 per cent of 3 year recoveries in papillary carcinoma, and 29.7 per cent in the infiltrating variety. In 127 cases based upon clinical diagnosis there were 55 per cent of 3 year recoveries in papillary carcinoma, and 27.8 per cent of 3 year recoveries in the infiltrating type. It will be seen, therefore, that from a prognostic point as to end-results the clinical diagnosis has been as valuable as the microscopic.

Waters reported on 120 cases treated by deep roentgen therapy up to 1926 (one case of sarcoma). He gives no final statistics but concludes that the best treatment for superficial papillary carcinoma is a combination of deep roentgentherapy and radium applied to the surface of the growth, while with the infiltrating growths, when operable, radical resection should be carried out. All others should be given a trial by deep roentgentherapy, perhaps associated with suprapubic cystotomy and implantation of radium needles.

Grier reported on 17 inoperable cases with 3 recoveries, treated by deep roentgentherapy.

Burnam reports on 186 cases of tumors of the bladder treated by irradiation. Of these 88.2 per cent were malignant, and of the malignant cases 66 per cent were of the large inoperable type. Of the 111 large carcinomata, there were 11 cures (9.9 per cent) and of the 57 small carcinomata there were 20 cures (35 per cent). Of the 59 large and inoperable papillary carcinomata there were 7 cures (12 per cent) and 20 with palliative results. Of the 29 small and medium papillary carcinomata 9 were cured (31 per cent). Of the 49 large and inoperable infiltrating carcinomata there were 4 cures (8 per cent) with palliation in 13 cases. Of the 9 small and medium infiltrating carcinomata there were 5 cures (55 per cent) with palliation in 4 cases. Such results should make us consider irradiation in all cases of carcinoma of the bladder, and should make us all keen to improve our technique, conserve normal tissue, and do all possible to make a diagnosis early and treat thoroughly and skilfully from the beginning.

RESULTS IN OUR CASES

Our experience is limited to 83 cases of carcinoma of the bladder. All were advanced, large, and belong to the inoperable group. There were 63 males (75.9 per cent) and 20 females (24.1 per cent). The youngest was 36 and the oldest 78 years of age, giving an average of 57.2 per cent years. Judged by the history of symptoms the average duration of the disease was 15.3 months.

TABLE I.—SUPRAPUBIC CYSTOTOMY, ELECTROCOAGULATION, RADIUM NEEDLES—FORTY-THREE CASES

Name	Age	Date	Urologist	Duration	Results	Remarks
W. C.	72	4-27-16	E. LaPlace	2 weeks	Dead	1 year after treatment.
W. B.	59	5-11-16	E. LaPlace	6 months	Dead	1 year after treatment?
E. D.	48	3- 8-20	W. MacKinney	9 months	Dead	5 months after treatment.
T. M.	58	3-10-20	B. A. Thomas	6 months	Dead	1 year after treatment.
J. H. S.	65	5- 3-20	W. MacKinney	2 years	Alive	10 years after treatment.
M. S.	48	5- 4-20	W. MacKinney	8 months	Alive	10 years after treatment.
H. R.	62	7- 9-20	B. A. Thomas	1 year	Dead	1 year after treatment.
F. S.	63	10-19-20	B. A. Thomas	2 months	Dead	2 years after treatment.
Mrs. R.	52	11-10-20	W. MacKinney	6 months	Dead	6 months after treatment.
J. M.	50	12-21-20	B. A. Thomas	8 months	Dead	1 year after treatment.
C. B.	46	12- 8-20	John B. Deaver	6 months	Dead	1 year after treatment—cardiac disease.
D. S.	55	2- 2-21	W. MacKinney	1 year	Dead	*1-9 years after treatment—cause unknown.
T. B.	60	3- 1-21	W. MacKinney	3 months	Dead	1 year after treatment?
W. F.	60	5- 3-21	F. Brady	2 months	Dead	1 month after treatment.
B. F.	55	5- 4-21	Leon Herman	4 years	Dead	1 year after treatment.
H. W.	76	7- 7-21	B. A. Thomas	1½ years	Dead	2½ years after treatment.
K. G.	42	8-13-21	W. MacKinney	9 months	Dead	†2-5 years after treatment—accidental.
W. C.	51	8-22-21	W. MacKinney	2 years	Dead	4 months after treatment.
R. B.	72	9-14-21	W. MacKinney	1½ years	Dead	3 months after treatment.
S. H.	37	10-26-21	B. A. Thomas	7 months	Dead	2 months after treatment.
G. S.	69	10-29-21	G. P. Muller	2 weeks	Dead	‡3-7 years after treatment—cause unknown.
Mrs. H. S.	60	11-14-21	B. A. Thomas	2 years	Dead	1 year after treatment.
M.M. B.	68	11-16-21	James Kelly	1 year	Dead	1 month after treatment.
S. N.	61	12-16-21	B. A. Thomas	1 year	Dead	7 hours after operation.
Miss B.	36	12-23-21	B. A. Thomas	2 years	Alive	9 years after treatment.
H. T.	59	1-10-22	B. A. Thomas	14 months	Dead	8 months after treatment.
F. K.	65	3-17-22	B. A. Thomas	6 months	Dead	1 year after treatment.
Dr. C. R.	48	3-21-22	E. LaPlace	1 month	Dead	16 months after treatment
O. W.	46	4- 7-22	B. A. Thomas	9 months	Dead	17 months after treatment.
H. E.	57	6- 1-22	W. MacKinney	5 weeks	Dead	6 months after treatment.
Mrs. E.	58	6-29-22	B. A. Thomas	1 year	Dead	1½ years after treatment.
W. L.	70	11-23-22	B. A. Thomas	6 months	Dead	1 year after treatment.
J. B.	66	12- 1-22	B. A. Thomas	2 years	Dead	2 weeks after treatment.
A. MacK.	48	12- 4-22	S. McDowell	4 months	Dead	2 weeks after treatment.
Mrs. F.	50	12-18-22	Leon Herman	1 year	Alive	8 years after treatment—radium applied in vagina.
J. H.	79	3- 7-23	A. E. Burke	1 month	Dead	5 days after treatment.
Mrs. C.	65	7-31-23	C. MacFarlane	3 years	Dead	1 year after treatment.
G. N.	58	8-17-23	B. A. Thomas	6 months	Dead	1 year after treatment.
H. W. I.	59	9-21-23	E. LaPlace	5 months	Dead	9 months after treatment.
M. C.	53	9-21-23	B. A. Thomas	5 years	Dead	§1-6 years after treatment—cause unknown.
C. S.	75	7-17-25	C. MacFarlane	3 months	Dead	4 months after treatment.
Mrs. W.	68	2- 2-26	A. H. Lippincott	2 years	Dead	19 months after treatment.
S. C.	48	5- 7-29	B. A. Thomas	1 year	Dead	1 month after treatment.

4 cases living and symptom free, 9.3 per cent.
2 cases living and symptom free, 10 years
1 case living and symptom free, 9 years.
1 case living and symptom free, 8 years.
Four other cases lived from 5 to 9 years and died from unknown cause. Total recovery for more than 5 years. 7 out of 43 inoperable cases equals 15.6 per cent. Fig. 4, Case 2.

*Alive for 9 years after treatment (cause of death unknown).
†Alive for 5 years after treatment (accidental death).
‡Alive for 7 years after treatment (cause of death unknown).
§Alive for 6 years after treatment (cause of death unknown).

TABLE II.—COMBINED SURGICAL AND RADIATION TREATMENT

Growth Excised, Followed by X-ray Treatment—Seven Cases

Name	Age	Date	Urologist	Duration	Results	Remarks
Rev. G. R.	64	10-16-07	J. B. Roberts	2 years	Dead	1 year after treatment.
H. S.	68	8- 7-16	P. Pilcher	1 year	Dead	Probably died 1 year after treatment.
Mrs. G. R.	45	11-10-20	W. Babcock	5 years	Dead	3 months after treatment. Growth excised 4 years before X-ray treatment. Treated for recurrence.
P. C.	44	5- 5-23	E. E. Gladman	7 months	Dead	2 months after treatment.
W. S.	71	1-18-26	B. A. Thomas	7 weeks	Dead	1 year after treatment.
G. L.	52	4- 7-25	B. A. Thomas	1 year	Dead	1 year after treatment.
M. M.	48	9-15-27	John Jopson	5 months	Dead	6 months after treatment.

Remarks: These were large infiltrating carcinomata and the excision was probably not complete. The X-ray treatment "low-voltage" did not cure the remaining or recurrent disease.

Growth Excised, Followed by Radium Packs in Bladder and X-ray Treatment—Six Cases

Name	Age	Date	Urologist	Duration	Results	Remarks
Dr. S. B.	37	7- 3-17	C. Nassau	3 months	Dead	4 years after treatment. Recurrence.
Mrs. J. S.	59	2- 8-18	B. A. Thomas	3 months	Dead	1½ years after treatment.
J. S.	61	1-17-19	J. DaCosta	6 months	Dead	1 month after treatment.
T. B.	57	12-29-25	B. A. Thomas	3 years	Dead	1 year after treatment.
Miss B.	50	6- 9-26	B. A. Thomas	1½ years	Dead	2 months after treatment.
S. E.	54	1- 7-30	B. A. Thomas	3 years	Dead	6 months after treatment.

Exploratory Operation, No Removal, Followed by X-ray Treatment

Name	Age	Date	Urologist	Duration	Results	Remarks
V. M.	42	10-22-15	C. Bartlett	6 months	Dead	1 year after treatment.
I. S.	67	10- 9-28	Leon Herman	2 years	Dead	2 months after treatment.

Remarks: The review of these 15 cases of carcinoma which were still of a size that could be excised more or less completely show no cures in spite of the postoperative X-ray treatment "low-voltage" or treatment given for recurrence. This would seem to indicate that for the removal of the tumor the following methods are preferable.

The prostate was known to be involved by the tumors which were primary in the bladder in 5 cases out of the 63 males (7.9 per cent).

I am indebted to my associate Dr. Leo D. Parry for preparing the tables from my records. These tables show the classification of our cases of carcinomata of the bladder treated by irradiation. (See Table I.)

It must be realized that the 43 cases in Table I which were treated through suprapubic cystotomy were large inoperable carcinomata and while only 15.3 per cent of the recoveries passed the 5 year period it represents some progress. The technique for these procedures has been previously described in detail by the late B. A. Thomas and myself. While there were only 15.3 per cent of 5 year recoveries, there were more temporary recoveries. However, it is my present impression from theoretical grounds and a few recent cases that the insertion of radium needles can be replaced to advantage by highly filtered radium units in the form of small packs within the bladder. (See Tables II, III, IV, V, VI, VII.)

SUMMARY AND CONCLUSIONS

1. Pneumocystography is a valuable means of determining the presence, size, outline, position, and amount of infiltration of a carcinoma of the bladder.

2. It can be carried out by any careful roentgenologist with sterile catheter, atomizer bulb, and a hæmostatic forceps.

3. Radiotherapy involves treatment by radium in the form of capsules, needles, or seeds (glass or gold), and by the use of deep roentgentherapy either alone, or before, or after electrocoagulation.

TABLE III.—ELECTROCOAGULATION AND RADIATION THERAPY

Growth Electrocoagulated Through Suprapubic Cystotomy, Followed by Radium Packs in Bladder and X-ray Treatment—Five Cases

Name	Age	Date	Urologist	Duration	Results	Remarks
F. J.	52	4- 7-19	E. LaPlace	2 months	Dead	1 year after treatment.
M. W. S.	69	7-10-19	B. C. Hirst	6 months	Dead	18 months after treatment.
N.	52	8- 1-19	E. LaPlace	2 years	Alive	11 years after treatment.
L.	62	11-18-29	W. MacKinney	10 months	Dead	7 months after treatment. Apoplexy—1 day after operation.
G.	54	6- 9-30	J. C. Birdsall	1 year	Alive	7 months after treatment.

Remarks: These 5 large inoperable growths were treated by radium capsules (rather crudely in 3) packed against the diseased area. Of these cases, 1 remained symptom free 11 years and another 7 months.

Electrocoagulated Cystoscopically, Followed by X-ray and Radium Treatment—Eight Cases

Name	Age	Date	Urologist	Duration	Results	Remarks
G. L.	54	1- 5-15	I. V. Levy	4 months	Dead	13 months after treatment.
A. S. E.	63	5-17-16	W. MacKinney	1 year	Dead	7 months after treatment.
O. A. K.	56	2-14-24	B. A. Thomas	2 years	Alive	7 years after treatment.
A. T.	52	3-21-25	W. Haines	6 months	Alive	2½ years after treatment.
M. L. M.	70	5-14-25	B. A. Thomas	6 months	Alive	5 years after treatment.
N. C.	65	9-15-25	B. A. Thomas	10 years	Dead	1 year after treatment.
Mrs. E. B.	74	12- 3-26	D. P. Pelouse	2 years	Dead	11 months after treatment.
Mrs. B. Y.	63	2-28-27	B. A. Thomas	4 years	Dead	11 months after treatment.

Remarks: Of these 8 cases, 3 became symptom free—37.5 per cent (7, 5, 2½ years). The fourth of these cases is one of my patients who had also had carcinoma of the penis and is well and working every day (Fig. 3). This latter group represents the more favorable group because of the smaller and less infiltrating type. My impression with our present knowledge is that when practical, and in the earlier and smaller lesions, the intravesical destruction associated with "high-voltage" X-ray treatment is the best procedure.

TABLE IV.—IRRADIATION ONLY—TWELVE CASES

Name	Age	Date	Urologist	Duration	Results	Remarks
R. B.	59	10-29-15	A. J. Sibbel	2 months	Alive	15 years after treatment.
Judge M.	76	5-16-16	E. LaPlace	1 year—inop.	Dead	1 year after treatment.
J. C.	57	9-29-22	Leon Herman	2 years—inop.	Dead	1 year after treatment.
G. O.	52	1-15-23	Leon Herman	6 months—inop. metastasis	Dead	7 months after treatment.
Mrs. M. B.	63	3-27-23	W. L. Estes	1½ years	Dead	9 months after treatment.
G. S.	63	12-29-25	B. A. Thomas	1½ years	Dead	1 year after treatment.
Mrs. G. F.	51	3-25-26	W. MacKinney	8 months	Dead	4 months after treatment.
A. D. W.	66	8-12-26	C. DeShivers	4 years	Dead	4 months after treatment.
Mrs. E. K.	59	6-20-27	J. B. Lownes	8 months	Alive	3½ years after treatment.
G. K.	38	5- 8-29	B. A. Thomas	1 month	Dead	1 year after treatment.
H. T.	58	1- 6-30	Thos. McCrae	7 years	Alive	1 year after treatment.
Mrs. G. S.	55	6-13-30	James Anders	2 years	Alive	7 months after treatment. Symptom free—radium applied in vagina.

Remarks: Of these 12 cases, 4 are symptom free (15, 3½, 1 years, 7 months), 33⅓ per cent. Three of these 4 cases have been treated by "high voltage" treatment, while the other was treated by "low voltage" X-rays. In women, especially when the tumor occupies the neck of the bladder or the posterior wall, one can get additional help by highly filtered gamma radiation (2 millimeters platinum) applied by pack into the vagina (Case 3, Figs. 5, 6, 7). In spite of the fact that most of these cases were treated by earlier and less perfect technique, the percentage of recoveries is nearly equal to those early cases in which the growth was destroyed cystoscopically, proving that the irradiation has value independent of the electrocoagulation (Figs. 8, 9, 10, Case 4, and Figs. 11, 12, Case 5).

TABLE V.—DURATION OF LIFE AFTER TREATMENT BY ALL METHODS

	Cases
6 months or less	26
8 months or less	7
1 year	27
1 year 6 months	6
2 years	3
3 years	1
4 years	1
5 years	2
6 years	1
7 years	2
8 years	1
9 years	2
10 years	2
11 years	1
15 years	1
Total	83

	Cases	Of total	Per cent
Symptom free 3 years or more	14	79	17.7
Still under observation—symptom free (X-ray, operation, and radium packs)	1		
Symptom free 5 years or more	12	78	15.3
Still under observation—3 years	1		

	Cases
Operation—resection of growth, or electro-coagulation and insertion of radium needles	71
Not operated upon but treated with X-ray or radium only	12
Living and well at end of 15 years	1
Living and well at end of 3 years	1
Living and well at end of 2 years	1
*Living and well at end of 1 year	1
*Living and well at end of 7 months	1

*Still under observation but symptom free.

TABLE VI.—OUTLINE OF IRRADIATION TREATMENT GIVEN IN SOME CASES WITH GOOD RESULTS

Name	Age	Date	Urologist	Symptom free	Treatment
1. R. B.	59	10–29–15	A. Sibbel	15 years Living	625% X-ray through 12 fields anterior. 425% X-ray through 8 fields posterior.
2. Dr. S. B.	37	7– 3–17	C. Nassau	3½ years Died of rec. carcinoma	Excision of growth; 375% X-ray through 4 fields anterior; 275% X-ray through 2 fields posterior. Operation: electrocautery; radium packs in bladder 750 mg. hrs. ½ mm. silver and rubber, 1 cm. distance—100% X-ray through 2 fields anterior; 100% X-ray through 2 fields posterior.
3. N. C.	57	8– 1–19	E. LaPlace	11 years Living	Growth destroyed by cautery—900 mg. hrs.—radium capsule, 1 mm. brass and rubber, 2 cm. distance, 9 hours.
4. J. H. S.	65	5– 3–20	W. MacKinney	10 years Living	Electrocoagulation of growth—800 mg. hrs.—needles inserted into base of growth.
5. M. S.	48	5– 4–20	W. MacKinney	10 years Living	Electrocoagulation—640 mg. hrs., needles inserted—100% X-ray through 4 portals, crossfire. Had a recurrence and Dr. T. Stelwagon operated upon bladder.
6. D. S.	55	2– 2–21	W. MacKinney	9 years Died—cause unknown	Electrocoagulation—1,040 mg. hrs., needles inserted into base of growth. 500% X-ray through 1 field anterior. 350% X-ray through 1 field posterior. Low voltage used.
7. K. G.	42	8–13–21	W. MacKinney	5 years Accidental death	Electrocoagulation of growth—1,620 mg. hrs. Radium. Needles inserted around base of tumor.
8. G. S.	69	10–29–21	G. P. Muller	7 years Died—cause unknown	Electrocoagulation of growth—1,440 mg. hrs., radium needles inserted around base of growth.
9. Mrs. E. B.	36	12–23–21	B. A. Thomas	9 years Living	Fulguration of growth—240 mg. hrs., needles inserted. 240% X-ray cross fire through 4 fields.
10. Mrs. S. F.	50	12–18–22	Leon Herman	8 years Living	625% X-ray cross fire through 4 portals. Fulguration of growth—640 mg. hrs., radium needles inserted into base of growth—1,200 mg. hrs., vaginal tampon, filtration was steel needles and 1 brass, 1½ cm. distance.
11. M. C.	53	9–21–23	B. A. Thomas	6 years Died—cause unknown	Electrocoagulation of growth—990 mg. hrs. of radium. Needles inserted around the base of growth.
12. O. A. K.	56	2–14–24	B. A. Thomas	7 years Living	Electrocoagulation—6,925 mg. hrs. in forms of packs on bladder (Congenital extravasation). 340% X-ray, cross fire through 4 portals.
13. M. M.	70	4–14–25	B. A. Thomas	5½ years Living	Fulguration of growth. 100% X-ray through 4 portals.
14. Mrs. E. K.	59	6–20–27	H. J. Tumen	3½ years Living	200% X-ray through 1 anterior field. 350% X-ray through 2 posterior fields. High voltage with 0.5 cm. copper and 2 al. used.
15. A. T.	52	6– 9–28	W. Haines	2½ years Living	Electrocoagulation of growth cystoscopically. 395% X-ray through 2 anterior portals. 280% X-ray through 2 posterior portals. 0.5 cm. used for 50% of treatment. 2 mm. cu. used for 50% of treatment.
16. H. T.	58	1– 6–30	T. McCrae	1 year Living	325% X-ray through 1 field anterior. 800% X-ray through 2 fields posterior.
17. Mrs. G. S.	55	6–13–30	James Anders	7 months Living	700% X-ray through 3 anterior portals. 492% X-ray through 2 posterior portals. 2 cm. copper filtration used. 2,400 mg. hrs. pack in vagina. 2 platinum—2 cm. distance.

TABLE VII.—LOCATION AND EXTENT OF DISEASE, WITH GOOD RESULTS IN EIGHTEEN CASES

Name	Age	Date	Urologist	Findings	Biopsy	Operation	Treatment	Results
R. B.	59	10–29–15	A. Sibbel	Entire trigone involved	None	None	X-ray	Living 15 years.
Dr.	37	7– 3–17	C. Nassau	Mass size of orange	None	Yes	Radium coagulation. X-ray	Died carcinoma 4 years.
N.C.	57	8– 1–19	E. LaPlace	Posterior wall involved	None	Yes	Cautery Radium needle	Living 11 years.
J. H. S.	65	5– 3–20	W. MacKinney	Left side of bladder involved	Yes Papillary carcinoma	Yes	Coagulation Radium needle	Living 10 years.
M. S.	48	5– 4–20	W. MacKinney	Left side bladder 2½ inches in diameter	None	Yes	Coagulation Radium needle X-ray	Living 10 years.
D. S.	55	2–21–21	W. MacKinney	Mass 6 inches in diameter	Yes	Yes	Coagulation Radium needle X-ray	Dead 9 years—cause unknown.
K. G.	42	8–13–21	W. MacKinney	Mass (cauliflower) on posterior wall	Yes	Yes	Coagulation Radium needle X-ray	Dead 6 years—accidental.
G. S.	69	10–29–21	G. P. Muller	Mass on posterior wall 5 by 4 cm.	None	Yes	Coagulation Radium needle	Dead 7 years—cause unknown.
Mrs. E. B.	36	12–23–21	B. A. Thomas	Posterior wall involved	Yes Papillary carcinoma	Yes	Coagulation Radium needle X-ray	Living 9 years.
Mrs. F.	50	12–18–22	Leon Herman	Neck of bladder involved 3 cm. in diameter	None	Yes	Coagulation Radium in vagina N. X-ray	Living 8 years.
M. C.	53	9–21–23	B. A. Thomas	Mass on left side 5 by 6 by 7 cm.	None	Yes	Coagulation Radium needle	Dead 5 years—cause unknown.
O. A. K.	56	2–14–24	B. A. Thomas	Exstrophy of bladder mass size of hen's egg	Yes	No	Coagulation Radium	Living 7 years.
M. L. M.	70	4–14–25	B. A. Thomas	Size of lemon	Yes	Yes	Coagulation Radium needle X-ray	Living 5 years.
E. K.	59	6–20–27	H. J. Tumen	Size of lemon posterior wall	None	None	X-ray	Living 3½ years.
A. T.	52	6– 8–28	W. Haines	Size of walnut	Yes (Rem. by cyst ex.)	None	X-ray Coagulation	Living 2½ years.
H. T.	58	1– 6–30	T. McCrae	Growth size of silver dollar	Yes (Rem. by cyst ex.)	None	X-ray	Living 1 year.
G. S.		6– 9–30	J. Birdsall	Left posterior wall 8 cm. by 6 cm.	None	Yes	X-ray Radium	Living 6 months.
Mrs. G. S.	55	6–13–30	James Anders	⅓ bladder involved	None	None	X-ray Radium in vagina	Living 7 months.

4. It seems that electrocoagulation is better than excision, followed by radium or X-ray treatment.

5. Some very encouraging results have been obtained by irradiation alone. Under such treatment the patient is usually relieved of hæmorrhage and pain. If our results can be made permanent and our percentage of cures increased, and if in the early stages the growth can be destroyed cystoscopically, it will be a great step in advance.

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EMPYEMA WITH BRONCHIAL FISTULA SIMULATING LUNG ABSCESS AND BRONCHIECTASIS[1]

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THE clinical manifestations of empyema with bronchial fistula are so different from those of uncomplicated empyema that from the diagnostic point of view it deserves separate consideration. While the latter presents itself usually as an obvious pleural disease, the former, because a cough productive of large quantities of sputum is its outstanding symptom, is apt to be confused with diseases of the lungs and bronchi. This is especially so when the empyema is small and encysted, in which case the physical and roentgenographic signs are usually atypical. It has seemed worth while to call attention to this diagnostic problem and by citing cases point out the many similarities and the few essential differences between this condition and lung abscess, bronchiectasis, phthisis, and other pulmonary diseases.

Rupture of a tuberculous cavity into the pleura is by far the most common cause of empyema with bronchial fistula.[2] Lung abscess and gangrene frequently produce it. A superficial pulmonary infarct, instead of regaining its circulation may die and be sloughed off, leaving a pulmonary defect with multiple bronchial openings into the pleura. Infection always either exists or supervenes. The condition may follow wounds of the lung and pleura although this is a much less frequent complication than one might expect. Spontaneous drainage of an unrecognized empyema whatever its origin is more likely to be by way of a bronchus than through the parietal pleura. Laennec, while he saw but one case of empyema necessitas, saw many of empyema with bronchial fistula. Cases have been reported in which a simple serous effusion eventually eroded the lung and invaded a bronchus. Pulmonary cancer, hydatids of the lung and pleura, bronchiectasis, and foreign body in the bronchi are rare causes.

When an empyema is draining through a bronchus, the physician, confronted with a patient raising quantities of sputum, often foul, is led to consider pulmonary rather than pleural pathology and to make a diagnosis of lung abscess, bronchiectasis, or tuberculosis. Even to one suspecting the condition the diagnosis is difficult.

If the empyema is acute, lung abscess is closely simulated. The two conditions produce practically identical symptoms. In both there is persistent cough, copious, often foul sputum, fever, night sweats, and all of the other manifestations of acute sepsis. The histories in both conditions present similar incidents: the onset, either sudden or gradual, with fever, pleuritic pain and slight non-productive cough, the sudden rupture of the abscess with the coughing up of a flood of pus, and the subsequent slight improvement with the establishment of partial drainage. If the empyema has been preceded by a typical pneumonia, the diagnosis is less difficult, but even here one is influenced to believe that it is an abscess rather than an empyema which has complicated the acute disease. If, however, the pneumonia has been atypical or the empyema has been caused by a small peripheral lung abscess or infarct, as is not infrequently the case, there is little in the history to distinguish the two conditions.

While the classical physical and roentgenographic findings of empyema and lung abscess are radically different, actually the findings are rarely classical, often similar. In lung abscess the surrounding pneumonitis often hides the cavity on the roentgenograms and the practical occlusion of the bronchus draining it, makes the physical findings those of atelectasis (flatness, absent breath sounds, and decreased fremitus), signs indistinguishable from those of fluid. If a fluid level is seen on the roentgenograms it is frequently difficult to say whether it is in an encapsulated pyopneumothorax or in a parenchymal abscess.

If the patient with empyema with bronchial fistula survives the acute stage of the disease and the cavity is not obliterated spontaneously, a chronic condition is established which is with difficulty distinguished from bronchiectasis. The characteristics of bronchiectasis are the periodic expectoration of large quantities of purulent sputum, the patient being free of fever and the other symptoms and signs of sepsis. In empyema with a bronchial fistula, as the walls of the cavity become thickened, absorption through them is reduced to a minimum. As this takes place the fever disappears and the patient improves gradually in nutrition and general health. The inflammation and swelling in the efferent bronchus,

[2] In the discussion of this paper this statement was contradicted. In a series of 24 cases reported by Emerson 18, or 75 per cent, were caused by tuberculosis. Statistics reported by Lebert show that between 5 and 10 per cent of all fatal cases of pulmonary tuberculosis are complicated by pneumothorax, many of which have patent fistulæ. Emerson, C. P., Johns Hopkins Hospital Reports, 1903—page 1.

[1] Read before the Chicago Surgical Society, February 6, 1931.

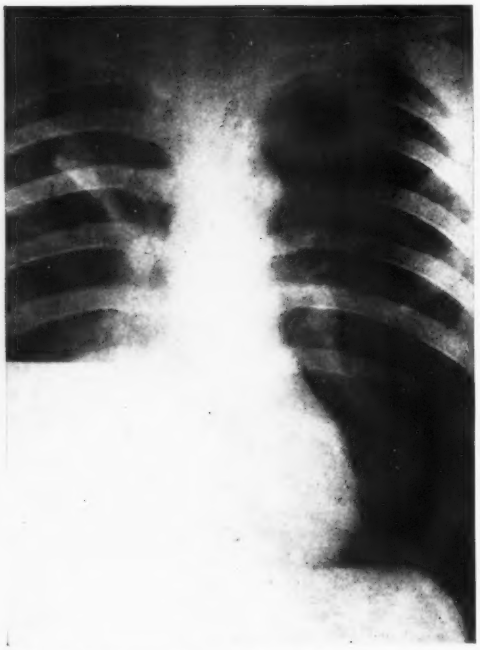

Fig. 1. Pyopneumothorax with bronchial fistula. Roentgenogram taken before operation. Case 1.

Fig. 2. Pyopneumothorax with bronchial fistula. Lateral roentgenogram showing cavity in approximation with posterior thoracic wall. Case 1.

which have hindered drainage and made the cough persistent, subside, and the cough, like that of the bronchiectatic, occurs only when the pus in the cavity has risen to the level of the bronchial opening. As in bronchiectasis the emptying spells are usually brought on by change in position or by exertion.

Fortunately, in most instances, the two conditions are readily identifiable by the physical and X-ray findings. In uncomplicated bronchiectasis these are few. The physical findings are slight dullness and coarse non-consonating râles found usually at one or both bases posteriorly, and the X-ray findings are merely an increase in the linear peribronchial markings. The variations from normal are often scarcely detectable.

In empyema with bronchial fistula, on the other hand, the findings are those of encapsulated air and fluid in the pleural cavity. If these are extensive and classical, the shifting dullness with tympany above it, the absent or amphoric breath sounds, and the succussion splash are easy of recognition.

Not infrequently, however, the empyema is small and loculated and the expected signs as well as the fluid level on the roentgenograms are masked by pleural thickening. Such cases can easily be confused with those types of bronchiectasis in which there is parenchymal fibrosis or atelectasis or in which the main bronchus is so constricted that the lung becomes drowned with secretions. In this variety of bronchiectasis, if the bronchus is patent, the even increase in density of parenchymal fibrosis or atelectasis can be differentiated from that of fluid by the physical examination which in the former shows the increased signs of consolidation rather than the decreased ones of fluid. If the bronchus is not patent and the lung is drowned and airless, the differentiations must be made by the demonstration of the bronchial occlusion. This can be done either by diagnostic bronchoscopy or by roentgenograms taken after the injection of iodized oil, or by exploratory thoracentesis. The location of the heart is also of great importance in this connection. In fibrosis or atelectasis it is drawn toward the affected side while in the presence of fluid it is forced in the opposite direction.

Because the treatment of the possible conditions is so different, a correct diagnosis is of the utmost

Fig. 3. Roentgenogram taken after drainage of the empyema. Case 1.

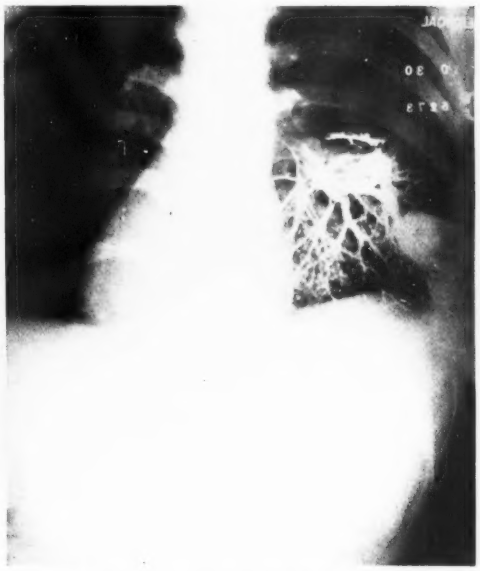

Fig. 4. Roentgenogram taken after the injection of iodized oil into the sinus which persisted after operation. Demonstration of bronchial fistula. Case 1.

importance. If there is a lung abscess, exploratory aspiration, with the risk of empyema, is dangerous. Expectant treatment with salvarsan and postural drainage and later, if necessary, thoracotomy, are indicated. If it is bronchiectasis, vaccines, lipiodol injections, postural drainage, and perhaps phrenicectomy are indicated. None of these procedures, nor the regimen for pulmonary tuberculosis, can possibly benefit an empyema, which in most instances can be cured by a simple rib resection. It is a tragedy for a case of this kind to go for 8 years, as did one of those reported below, with diagnoses of lung abscess, bronchiectasis, and pulmonary tuberculosis when he could have been cured in 2 months by the resection of a rib.

Each case is a specific problem. Success in diagnosis will depend first upon recognition of the frequency of the condition and consideration of its possible presence; second, upon a careful history and physical examination; and, third, upon the interpretation of the roentgenograms. These should always be taken with the patient in an upright position and in the anteroposterior, lateral, and oblique positions. If these positions are used, one can demonstrate whether or not there is a fluid level and whether or not it extends to the chest wall. Plates taken after the injection of iodized oil are practically essential. If the case is one of bronchiectasis or bronchial occlusion, there is no further doubt as to the diagnosis. In lung abscess there is usually revealed a wedge shaped filling defect in the parenchyma with its apex toward the hilus. In empyema with fistula the lung is shown pushed away from the chest wall.

If after all diagnostic methods have been tried there is still a question as to whether the condition is empyema or lung abscess, exploratory thoracotomy should be performed without a preliminary diagnostic aspiration. I have already pointed out the danger of producing an empyema if aspiration is performed in the presence of a lung abscess.

It has been the purpose of this paper to discuss the diagnosis of empyema with bronchial fistula, not the treatment. In general the treatment is the same as that of uncomplicated empyema. The presence of the fistula contra-indicates closed drainage and irrigations and makes rib resection the operation of choice. This is further indicated in that the temporary partial collapse of the lung favors the healing of the fistula. If the process is recognized and drained in its acute stage, both the cavity and the fistula will, in most instances, heal without further interference. If the fistula fails to close a sinus will persist. That it is the fistula which is causing the sinus can be demonstrated by roentgenograms taken after the injection of iodized oil. If the oil is injected into the sinus the

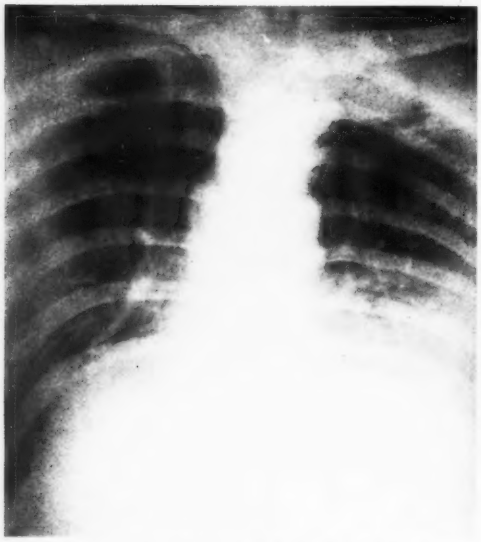

Fig. 5. Pyopneumothorax with bronchial fistula. Roentgenogram taken before operation with the patient in the supine position. No fluid level is seen. Case 2.

Fig. 6. Roentgenogram taken before operation with the patient in the standing position. A fluid level extending to the thoracic wall in the axillary line was visible. Case 2.

plates will show filling of the bronchial tree in the affected region. Such a fistula can be closed only by dissecting out the tract to the surface of the lung, exposing an area about the bronchial opening, and cauterizing the lips of the fistula with silver nitrate. The wound is packed wide open and the cauterization repeated every week or ten days until the granulations have closed the opening.

If the empyema has become chronic the procedure is the same until the cavity has ceased to decrease in size and until the patient's condition has improved sufficiently to permit one of the operations indicated for chronic empyema.

Case 1. Mr. J. D., a white insurance agent 40 years old, was first seen at the Augustana Hospital in consultation with Dr. Grosz on February 15, 1930. His complaints were cough with the production of large quantities of foul sputum, weakness, fever, and night sweats of six weeks' duration.

The patient said that he had always been subject to colds which followed one after the other most of the winter. He was perfectly well and had no cough during the summer. Two months before he was first seen, he developed a head cold and a few days later it "settled on his chest." Instead of continuing as a chronic cough, as it had previous winters, it grew gradually worse and he began to lose weight and run a slight fever. About 2 weeks after it started he suddenly coughed up several mouthfuls of blood. This had a foul odor. The same thing occurred a few days later. Following this his sputum gradually increased in amount and became very foul. He stopped work and entered the hospital on January 1, 1930. He grew steadily worse and continued running a fever of 102 to 103 degrees every afternoon.

Examination on February 15 showed a markedly emaciated, middle aged man sitting up in bed and coughing almost incessantly. His cheeks were sunken and flushed. The temperature was 102 degrees and the pulse 110. The only abnormal physical findings were in the chest. There was marked limitation of motion of the right hemithorax. At the right base posteriorly from the angle of the scapula downward, percussion note was flat and the breath sounds and tactile fremitus were absent. Above this was an area either of tympany or Skodaic resonance.

The roentgenogram taken in the anteroposterior position (Fig. 1) showed what appeared to be a large cavity with a fluid level in the right lower lung field. The lateral plate (Fig. 2) showed that this was in the posterior part of the thoracic cavity and in approximation with the posterior chest wall.

A diagnosis of empyema with bronchial fistula was made. Because there was a difference of opinion as to whether it was a lung abscess or an empyema, aspiration was not performed. Under local anæsthesia the ninth rib in the midscapular line on the right was resected. Careful incision of the rib bed led into a large empyema cavity from which about a pint of foul pus, similar to that which the patient had been raising, was aspirated. Open drainage was established by inserting two large soft rubber tubes into the pleural cavity.

The patient stopped coughing immediately after the operation. At the end of a week his temperature was normal and he was well on the road to recovery. The drainage tubes were kept in place for about 6 weeks and then gradually shortened and withdrawn, the roentgenogram having shown that the cavity was obliterated.

The sinus in the chest wall persisted and when the patient forced his expiration air could be heard coming

Fig. 7. Pyopneumothorax with bronchial fistula. Roentgenogram taken before operation showing multiple fluid levels. Case 3.

Fig. 8. Pyopneumothorax with bronchial fistula. Lateral roentgenogram taken before operation. Case 3.

through it. Roentgenograms taken after injection of the sinus with lipiodol showed that it led into a bronchus (Fig. 3). The patient was told to go back to his work and return in 6 months if the sinus was still present. At the end of 3 months it had closed and has remained so to the present time.

CASE 2. Mr. J. W., a white mine operator of 52 years, was first seen in consultation with Dr. Hollands and Dr. I. H. Chilcott at the Illinois Masonic Hospital on August 4, 1930. His complaints were cough productive of large quantities of foul purulent sputum, fever weakness, and sweats of 1 month's duration.

Two and one-half months before he was first seen, he developed a bothersome dry cough. This did not make him sick in any way and he continued about his work. One month later he was wakened suddenly at night by a terrific pain in his right hemithorax. The pain was very severe and he was unable to get his breath. The next day he suddenly coughed up a flood of very foul sputum mixed with blood. By evening of that day his temperature had risen to 104 degrees. He improved somewhat after this but continued to be very ill.

Physical examination showed a large, well developed elderly man lying in bed and coughing incessantly. His temperature was 102 degrees, pulse 120, respirations 28. There were no abnormal findings save in the chest. The motion was practically equal on the two sides. The heart was displaced slightly to the left. At the right base anteriorly there was an area of dullness the upper border of which ran from the cardiohepatic angle upward and outward to the right nipple and then downward to meet the liver dullness again in the midaxillary line. Over this area the breath sounds and tactile and vocal fremitus were absent. Red blood cell count was 3,700,000; hæmoglobin, 60 per cent; white blood cells, 13,700.

The roentgenogram which had been taken with the patient in the supine position showed an even increase in density at the right base with a hazy upper border which

Fig. 9. Roentgenogram taken after operation. The multiple fluid levels were in the same empyema cavity. Case 3.

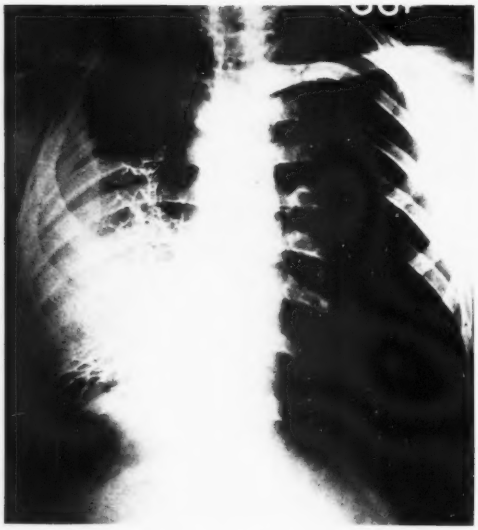

Fig. 10. Pyopneumothorax with bronchial fistula. Roentgenogram taken before operation. Iodized oil has been injected to determine whether the lesion was intrapulmonary or extrapulmonary. Thickening of the pleura masks the fluid level. Case 4.

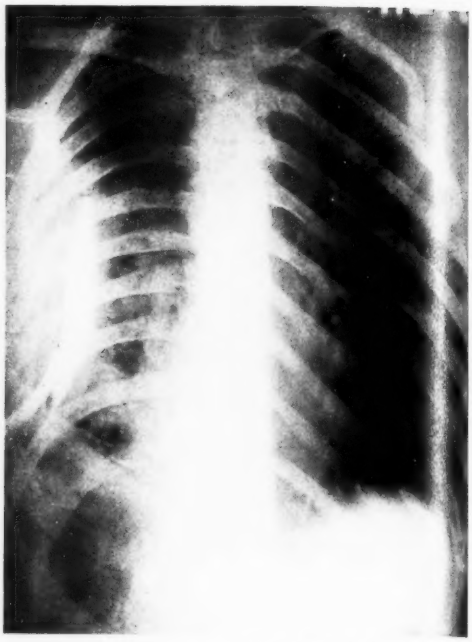

Fig. 11. Roentgenogram taken after drainage of the empyema. Iodized oil has been injected into the cavity to demonstrate its outline. Case 4.

rose slightly in the axilla. Although the patient was extremely weak he was taken to the X-ray department and, after iodized oil had been injected, was supported in an upright position while another plate was exposed. This showed that there was no obstruction of the bronchus. Bronchiogenic carcinoma had been considered. It revealed also that the lung was pushed away from the chest wall and that there was a fluid level in the axilla between the lung and the ribs.

A diagnosis of empyema with bronchial fistula was made. On the operating table exploratory aspiration was performed, the needle being inserted in the fifth intercostal space on the right just below the nipple. Thick pus was obtained. Resection of a portion of the fifth rib at this site and incision of the parietal pleura led into a small loculated empyema cavity. Open drainage was established.

The patient ceased coughing immediately following the operation and has not coughed since. By the end of a week his temperature had fallen to normal and he was able to leave the hospital. The drainage tubes were kept in place for about 1 month and were then gradually withdrawn. The wound had healed completely 2 months after the operation. The patient has regained his normal weight and has no cough.

Case 3. Mr. G. W., a white structural steel worker, 48 years old, was seen in consultation with Dr. M. B. Burns at the Columbus Hospital on October 27, 1930. His complaints were cough productive of 23 ounces of foul purulent sputum each 24 hours, fever, weakness, and night sweats.

On August 20, 1930, while working at his trade, the patient fell several stories and broke both bones of his right lower leg. There was no injury to the chest or to other parts of the body. There was considerable displacement of the fragments and he was consequently kept in bed with his leg in traction. He had no cough or other complaint and his temperature was normal until about 1 month later he suddenly developed a severe pain in the right lower thorax. During the rest of the day he coughed a little and the next day developed a fever of 103 degrees and began raising considerable amounts of foul, purulent sputum. The sputum gradually increased in amount until in a few days he was raising 23 ounces a day. He continued growing gradually weaker, coughing incessantly and running an afternoon temperature of 102 degrees. His pulse ranged between 90 and 100 degrees.

A roentgenogram taken the day after the onset of his pain showed an even increase in density in the right lower lung field which is very characteristic of fluid in the pleural cavity. One taken 2 weeks later showed multiple cavities and multiple fluid levels. The lateral plate taken at this time is of particular interest in that it shows so excellently the positions of the cavities in the sagittal plane of the chest.

Physical examination made with the patient in the sitting position showed that there was flatness to percussion at the base of the right pleural cavity, the upper border of which ran horizontally forward from the angle of the scapula through the axilla to the sternum. Voice, breath sounds, and fremitus were markedly decreased over this area. There was another area of flatness just to the right of the sternum, the upper border of which ran outward from the sternum to the anterior axillary line. These levels of fullness shifted as the patient changed his position.

A diagnosis of empyema with bronchial fistula was made. The multiple fluid levels were believed to be in the same cavity and to be caused by pocketings of fluid in shifting

pleural adhesions. Such pictures are not uncommon in instances in which artificial pneumothorax is complicated by an effusion.

Aspiration had been performed unsuccessfully posteriorly by another consultant. For this reason and because the roentgenogram and the physical examination indicated that there was fluid in the lower thorax in the anterior axillary line, aspiration was performed at this point. Pus similar to that which the patient was raising was obtained.

Under local anæsthesia, a segment of rib was resected at this point. Incision through the parietal pleura led into a large empyema cavity containing pus and air. The pus was aspirated and open drainage was established. The patient stopped coughing immediately after the operation, and his temperature came down to below 100 degrees.

Ordinarily I do not hesitate to drain an empyema anteriorly so long as the incision is toward the base of the cavity. Wherever the opening, drainage may be made efficient by having the patient lie on the incision. This patient had difficulty in doing so because of the cast on his leg. He continued running a slight fever and it was necessary to irrigate the cavity carefully with hypochlorite solution to bring down his fever. The cavity is small and decreasing steadily in size 6 weeks after the operation.

CASE 4. Mr. J. G., a single white laborer, 32 years of age, came to the dispensary complaining of cough productive of large quantities of sputum.

Eight years before the patient had had an acute respiratory disease from which he had a prolonged convalescence. He was confined to bed for many months. During this time the cough which had been present from the start became increasingly productive until he was raising as much as 1 pint each 24 hours. He improved gradually in general condition and was eventually fever free and able to be up and about. His cough continued the same. Since that time he had been in fairly good health except for the very bothersome productive cough. This cough occurred chiefly in the morning when he got up and at night when he went to bed. It was also brought on by bending over or by exerting himself unduly. He had been told by different physicians that he had lung abscess, bronchiectasis, and pulmonary tuberculosis. He had been sent to Arizona and to California, but had failed to improve.

Physical examination revealed a relatively well developed and nourished adult male. The only important physical findings were those encountered in the chest. Extending from the apex to the base in the axilla and from the midclavicular line to the midscapular line was an area of dullness to percussion. Over this area the breath sounds were absent and the tactile and vocal fremitus greatly reduced.

The roentgenogram showed an area of greatly increased density occupying the entire axillary portion of the left lung field. The plate taken after the injection of iodized oil showed that the lung was pushed away from the chest wall. Aspiration gave thick yellow pus of the same variety that the patient was coughing up. Following the establishment of drainage by the insertion of a tube, the patient stopped coughing and has not coughed since. The empyema cavity decreased markedly in size but failing to close completely had to be obliterated by a Schede operation.

SUMMARY AND CONCLUSIONS

1. Empyema with bronchial fistula closely simulates lung abscess or bronchiectasis. The acute cases simulate lung abscess, the chronic ones bronchiectasis.

2. Four cases are presented in which the diagnosis was uncertain and difficult.

3. It is important to consider the condition in all cases presenting the symptoms of cough and copious sputum.

4. A careful history and physical examination and roentgenograms taken in the anteroposterior and lateral upright positions, before and after the injection of iodized oil, are essential to the diagnosis.

5. Diagnostic aspiration should not be performed for fear of infecting the pleura in case a lung abscess is present.

6. The treatment of empyema with bronchial fistula is drainage by rib resection. Closed drainage and irrigations are contra-indicated because of the bronchial opening.

7. In the acute cases the fistula and cavity will usually close spontaneously following drainage. If they do not, secondary operations are required.

OSTEOCHONDROMATOSIS OF THE KNEE JOINT[1]

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ACCORDING to Halstead the first systematic study of loose bodies in joints was done over three hundred years ago by Pechlin, a Swedish surgeon. Loose bodies may be composed of unorganized tissue, such as rice bodies, or made up of organized tissue, as cartilage, fibrocartilage, or bone.

Osteochondromatosis is a rare pathological process in which pedunculated and loose cartilaginous bodies are formed from the synovial membrane of joints, the knee being by far the most commonly affected. This condition is not to be confused with that of osteochondritis desiccans or osteochondral fracture in which the loose bodies arise from the articulating surfaces or in those cases of advanced osteoarthritis presenting loose bodies.

Lannaec, in 1831, is said to have first called attention to loose bodies arising from the membrane and he believed they came from the subsynovial tissues. In 1836, Brodie mentioned seeing several cases, and he felt that the process arose from the external surface or within the synovial membrane because the membrane could be seen to be reflected over the bodies before they became detached. This is in close agreement with the present conception of their origin. Brodie states: "In the museum of St. George's Hospital there is a specimen of a knee joint, the inner surface of which is lined by a great number of small pendulous excrescences, connected with the synovial membrane . . . and there is a reason to believe that the excrescences were the result of long continued inflammation of the synovial membrane."

Osteochondromatosis is usually monarticular and is commonly to be recognized in early or middle adult life, occurring in the following order of frequency; knee, elbow, shoulder, hip, ankle, and wrist. In a review of 19 cases by Jones, 12 were not over 40 and 8 were under 30 years of age. The 4 cases here reported were all in females under 45 years of age. The majority of cases reported in the literature have occurred in males, substantiating to some degree the part trauma would appear to play in its etiology. Rixford has recently reported a case in a man of 69 years, and while it is commonly seen much earlier, no age period is exempt.

The exact cause has not been proved. The history and physical examination rarely tend to support the infectious theory. The cases here reported all gave a history of trauma to the joint which the patient thought marked the onset. In many of the cases reviewed, a similar finding was noted. One is therefore impressed with the fact that it must be an important factor. It may not necessarily be direct trauma but irritation produced by wrenching or twisting of the joint. In 1907, Lexer advanced the idea that these osteochondromata arise from fully developed embryonal rests and pointed out the intimate developmental relationship of the synovial membrane to cartilage. The primitive connective tissue, which may normally persist in the region of the joint capsule, has been thought to give rise to cartilage which in turn can become ossified through irritation or infection. These loose bodies have therefore been thought by Geschickter to represent an overstimulation of a normal process. There would appear also to be some relationship between this process and various types of newgrowth. After an extensive study of its etiology and pathology, Jones states: "From a developmental standpoint one is led to the consideration of this process as one of the tumors." In considering the relationship of the synovial membrane to tumors in general, one is reminded of the fact that other neoplastic diseases arising from the membrane have been reported; for instance, fibromata, hemangiomata, and endotheliomata. The frequent history of trauma introducing their onset is not unlike the history of many neoplastic processes. Henderson has reported a case of osteochondromatosis of the knee joint associated with a malignant chondrosarcoma of the lower end of the femur of the same side. In this connection it may be of interest to note that in Case 4 operation had been done for an intestinal obstruction, at operation a huge megacolon being discovered, the exact cause of which was undetermined.

Histologically the joint capsule is composed of two layers, the outer stratum fibrosum and the inner stratum synoviale. It would seem that these cartilaginous rests begin to grow from the fibrous layer and push their way toward the joint cavity (see Fig. 8) growing to different sizes before being cast free into the joint. The question as to the portion of the joint first involved has been studied, and while any portion of the membrane may be the site, the junction of the joint capsule

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Fig. 1. Roentgenogram from Case 1, showing many loose bodies free within the knee joint.

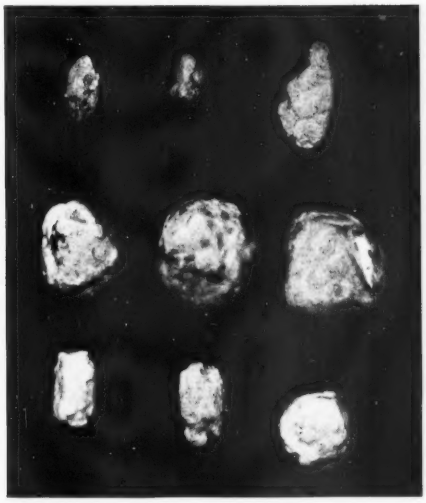

Fig. 2. Gross appearance of the loose bodies removed from the knee joint in Case 1.

and the periosteum has been noted to be frequently first affected. It is probable that the type of injury may be the deciding factor in the portion of the joint first involved.

In Case 1 when the joint was opened it was noted that the articular surfaces proper appeared quite normal but at the periphery of the femoral articular surface, at the junction of the synovial membrane and joint cartilage, were small attached osteocartilaginous masses which were thought to be loose bodies in the process of formation. In addition to these there were noted several similar masses attached to the synovial membrane in the suprapatellar pouch. In Case 3, we were able to obtain a roentgenogram taken 6 years before, which is here reproduced. On close inspection a few calcified areas can be identified in the posterior portion of the joint which would appear to be the beginning of the process in this case (see Fig. 5) and also illustrates the chronicity of this type of growth. While these ossifying papillomatous masses are attached, nutrition and growth can easily continue but when the bodies wander loose in the joint the question of their continued growth becomes one of speculation. They may receive nourishment by reattaching themselves temporarily to the membrane or from the joint fluid itself. Some of the earliest studies have indicated that the synovial fluid is not only a lubricant but also rich in proteins, inorganic salts, and sugar. In a study of loose bodies in joints Strangeways concludes that the constituents of the synovia are responsible for the changes observed in bone and cartilage with certain types of arthritis. Phemister points out that the synovia is enriched by irritation which the loose bodies produce. Certainly, as Forkner has recently observed, a need for further study and research of the normal and pathological joint fluid is evident. The growth is believed to be entirely limited to the cartilage and fibrous tissue cells in these aberrant masses as cross sections of the larger loose bodies have been reported as

Fig. 3. Photomicrograph showing cross section of one of the loose bodies in Case 1. Note the absence of any areas of calcification. Areas of poorly preserved cartilage with a center of degenerated tissue can be seen.

Fig. 4. Lateral roentgenogram of the right knee in Case 2, showing many loose bodies scattered throughout the joint.

Fig. 5. Roentgenogram taken 6 years ago of Case 3, showing an extremely early roentgenographic appearance of osteochondromatosis as characterized by a few indistinct calcified areas in the posterior pouch of the joint. The film shows this much better than the photograph.

showing only degenerated bone; in marked contrast to the microscopic appearance of the attached bodies, see Figures 9 and 10.

There appear to be at least two types of osteochondromatosis; first, those cases in which one or more, usually multiple, loose bodies are free within the joint. These may be of varying size—the largest in Case 1 was three-quarters of an inch in diameter—oblong or round with glistening white, cartilaginous surfaces, often pitted and presenting numerous bosses. When packed closely together definite facets may be formed and occasionally these bodies may be seen neatly packed together in the posterior pouch of the knee joint. Their tendency is to wander about, though they often gravitate backward during movement and produce remarkably few symptoms. The microscopic appearance of one of these loose bodies is shown in Figure 3. It is covered with a capsule of fibrous tissue and areas of poorly preserved cartilage cells scattered throughout. The absence of any area of calcification is striking.

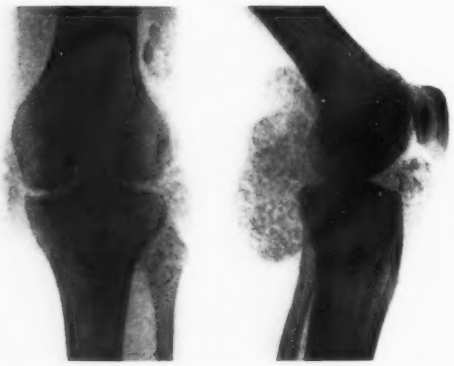

Fig. 6. Roentgenograms from Case 3, showing a late stage of the diffuse type of osteochondromatosis. Compare this with Figure 5 and note the absence of any articular change.

CASE 1. A woman, 32 years of age, came to the clinic on September 11, 1930, because of inability to extend the right knee. She gave no history of any definite trauma, although she had wrenched her knee several times within the last few years, with no ill effects. About 10 days before coming to the clinic, while scrubbing, she had felt a sharp pain in the knee and noticed that immediately after she was unable completely to extend the joint. She has had persistent pain and swelling of the joint since. This young woman was in good general condition. The right knee presented a rather glazed, shiny appearance and the normal contour of the joint was obliterated because of the swelling. There was an extremely sensitive point about the upper pole of the patella and when firm pressure was made over the patella the patient complained of pain in the joint. The knee was held in about 140 degrees and could not be extended beyond this point. Flexion could be accomplished to the complete range. No tenderness was present over the internal or external meniscus. Roentgenogram is shown in Figure 1.

Fig. 7. Photograph showing the gross appearance of a portion of the material removed from Case 3. A synovectomy of the anterior portion of the joint was done. *A*, the fat pad; *B*, a portion of the synovial membrane showing many attached masses.

The patient was admitted to the Orthopedic Service at Bellevue Hospital and operated on September 24, 1930. A curved incision was made along the medial border of the patella, under Esmarch, and the joint opened. Nine loose bodies were recovered, one large one being dislodged from the intercondyloid notch, with difficulty (see Fig. 2). The wound closed in layers and a firm pressure bandage was applied for the next 10 days. The wound healed *per primam* and at present the patient has a range of motion from 180 to 80 degrees, and complains of no pain or weakness in the knee.

CASE 2. A woman, 44 years of age, came to the clinic complaining of persistent pain in both knees for the past 18 years. The pain is worse in the right knee. She stated that 18 years ago she had fallen, striking rather heavily against the right knee. It had given her so much trouble that 9 years ago she had had a roentgenogram taken which had been pronounced negative. The pain in this case was quite marked.

This woman was in fair general condition. She had double knock knees and walked with both feet in abduction. There was crepitus on movement of both knees but very little restriction in movement. The patient felt that the pain was most marked in the right knee when she was going down stairs. She had very little swelling or local sensitiveness and gave no history of sudden sharp pain characteristic of a mechanical block. Roentgenogram of the left knee showed a mild degree of hypertrophic arthritis; this was more marked on the right and there were noted a number of loose bodies in the suprapatellar bursa and in the posterior portion of the knee joint. Removal was advised but the patient refused and did not return (Fig. 4).

Another and somewhat different type but thought to arise from the same underlying cause

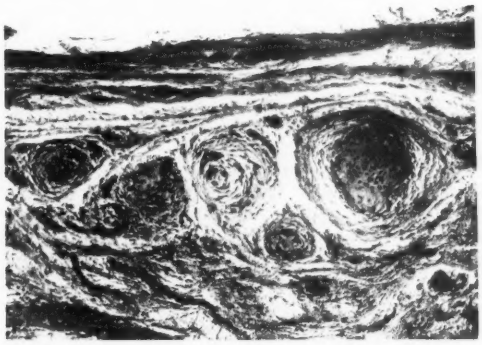

Fig. 8. Photomicrograph showing several early stages in the development of the osteochondromatosis in Case 3. Note the growing bodies that are here observed below the synovial layer.

is shown in Cases 3 and 4. Here the bodies, in great quantities, were found both free and attached, and this type would appear to resemble a neoplastic process more than the cases described. As these synovial chondromata become visible in the roentgenogram only after they calcify or ossify at their center in the pedunculated masses, the earlier cases must pass unnoticed for a while. Hesse describes a case that was not suspected until operation because of the negative findings. These 2 cases of the diffuse type here reported represent a late stage.

When the joint was opened in Case 3 a remarkable appearance was noted. The whole interior of the joint appeared studded with literally thousands of small, glistening, pearly white bodies about the size of seed pearls. They arose from every conceivable portion of the synovial membrane, even partially encroaching upon both semilunar cartilages. Many of these bodies were attached to the membrane by tiny stalks, others were free within the joint, and many had fused together, forming small clusters which popped out from the folds of the joint whenever it was moved (Fig. 10). The photograph shows the gross appearance very inadequately (Fig. 7). There was noticed a distinctly rancid odor from this disorganized joint. This observation, as far as the author has been able to discover, has not been mentioned in other cases reported but was so marked and distinct in this case that it is thought worthy of mention. Microscopically the sections of this case showed dense connective tissue through which are diffusely distributed many small circumscribed and encapsulated areas. These consist of fibrous connective tissue either completely or partially replaced by fibrocartilage

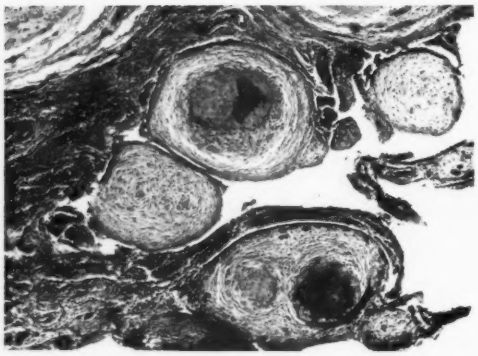

Fig. 9. Photomicrograph showing on the right a pedunculated osteochondroma with its long pedicle. The synovial membrane can be seen to be reflected over the mass which protrudes into the cavity. Other masses and evidences of a papillomatous synovitis are shown. Case 3.

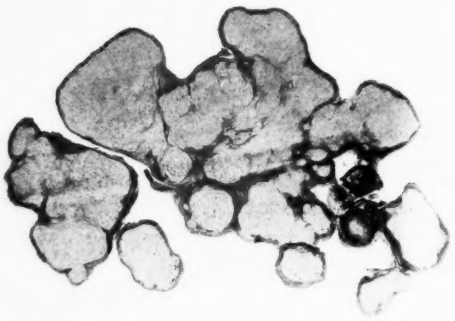

Fig. 10. Photomicrograph showing a cross section of several fused loose bodies removed from Case 3. No evidence of living bone tissue is seen but cartilage and fibrocartilage cells can be seen, evidence of the nutritive value of the synovia.

or bone. Some of these nodules can be identified below the synovial layer in varying degrees of development, before they have projected themselves into the joint cavity (Figs. 8 and 9). Many of these nodules project beyond the synovial surface and give the appearance of a chronic synovitis. The sections of this case were submitted to Dr. Ewing who stated: "It appears to be an ossifying papillomatous synovitis that has taken on the aspect of a benign neoplasm."

Case 3. A woman, 29 years of age, came to the clinic on October 9, 1930, because of stiffness in the right knee. About 6 years before the patient stated she twisted and wrenched the knee and shortly thereafter began to notice limitation of movement. She received baking and massage of the knee for several months. The knee was only moderately sensitive on movement and had no local heat (Fig. 5). This patient was a young woman in good general condition. The right knee was somewhat larger than its fellow particularly about the infrapatellar region and there was some atrophy of the right thigh muscles. The knee was held in an attitude of 170 degrees' extension. Any attempt further to extend it was restricted and painful. The joint could be flexed to 130 degrees without pain. The roentgenogram showed extensive, irregular, calcareous deposits, apparently all within the joint capsule, the largest mass being in the posterior portion of the joint capsule (see Fig. 6).

Fig. 11. Roentgenogram from Case 4 showing a diffuse type of osteochondromatosis of the knee joint. This case was not operated upon but the roentgenographic appearance is typical.

The patient was admitted to the Orthopedic Service of Bellevue Hospital and operated upon on October 22, 1930. The utility incision along the medial border of the patella was made under Esmarch and the joint opened. The gross appearance has been described above. A synovectomy as complete as possible was performed on the anterior portion of the knee joint. The wound was closed in layers and attempt made to dissect out the calcified masses in the posterior portion. This was unsuccessful. Both wounds healed *per primam* and the patient's convalescence was uneventful. When last seen in the clinic she had about 40 degrees' range of motion from an almost fully extended position and was able to carry on her housework without pain. This patient was not willing to have another attempt made for the removal of the posterior calcified masses and is being watched for any return of the process in the anterior portion of the joint.

Case 4. A woman, 40 years of age, was seen on December 15, 1930, complaining of stiffness in the left knee. She stated that 6 years ago she fell striking the left knee against the ground and badly twisting it at that time. The joint became swollen, with areas of ecchymosis over the anterior surface. She received baking and massage many times but the joint became increasingly stiff and painful. Roentgenograms taken a few months after the original injury were not available but the old report was negative save for a "synovitis." The knee has become quite stiff but at present is not painful. The patient feels, however, that the joint is weak.

This woman was in fair condition. She walked with the left knee slightly flexed, but complained of no pain. The

patient stated that she had been operated upon for an intestinal obstruction and presented a colostomy. Her general surgical record at Bellevue Hospital disclosed that she presented a huge megacolon, the exact cause of which is undetermined. Examination of the extremities revealed nothing unusual other than the left knee. The knee was held in an attitude of about 170 degrees' extension and there were only a few degrees of motion present. There was some enlargement of the joint but no synovitis or sensitiveness. Operation was advised but refused. (Fig. 11.)

In these 4 cases the absence of symptoms, other than those caused by mechanical blocking, was rather striking. None of the cases at the time of examination presented an increase in the joint fluid or local heat or redness. The chronic duration with a history of wrenching or twisting the knee followed by occasional sharp pain and increasing limitation in movement or a feeling of weakness about the joint was the usual history. Therefore the roentgenogram must still be regarded as the deciding factor in the diagnosis of osteochondromatosis.

The treatment is surgical. In the cases presenting multiple loose bodies, the removal relieves the mechanical obstruction. Sometimes this is technically quite difficult as the bodies may disappear deep into the joint or become lodged in the intercondylar notch of the femur as occurred in Case 1. Platt has suggested flushing the joint with saline under considerable pressure to loosen and dislodge elusive bodies. It is also helpful to make a careful pre-operative examination of the roentgenogram, counting the loose bodies at the time of operation, to see if these tally with those noted in the roentgenogram. In the diffuse type of the disease, a synovectomy as complete as possible would appear to be the method of choice. A curved incision along the medial border of the patella, the so called utility incision, permits an extremely satisfactory view of the anterior portion of the knee joint, with the minimum amount of bleeding. For exposure of the posterior portion of the joint, one may use the posterolateral or posteromedial incision described by Henderson or the popliteal approach advocated by Brackett and Osgood.

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THE OPERATIVE MORTALITY AND MORBIDITY OF PARTIAL GASTRECTOMY FOR PEPTIC ULCER

As Observed at the Klinik Eiselsberg, 1924–1930

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THERE exists today a voluminous literature concerning every phase of the subject of the medical and surgical treatment of peptic ulcer of the stomach and duodenum. Nevertheless, because of the wide divergence of opinion contained therein, it would seem of value to report statistically the results immediate or late of any large series of cases submitted to treatment by any single procedure. From the aspect of surgery this has been done excellently in the symposium on treatment of ulcer in the *Annals of Surgery*[1] where the results of various large American clinics have been made known. Inasmuch as the consensus of opinion favored gastroenterostomy, particularly for duodenal ulcer, it seems worth while to bring out some of the results of more radical surgery obtained in European clinics and more specifically the mortality and morbidity rates observed at the I. Chirurgischen Universitaetsklinik in Vienna (Vorstand Prof. Eiselsberg).

For this purpose 606 consecutive cases of peptic ulcer observed between January 1, 1924 and January 1, 1930 and treated by gastric resection, will be presented. The statistics shown were obtained from the clinical course from operation to hospital discharge.

As the scope of this work is largely statistical, no attempt will be made to review, in detail, the literature of gastric resection of ulcer. Excellent reviews are to be found in the different publications of Finsterer, von Haberer,[2] Starlinger,[3] and others.

This series comprises 449 cases of ulcus duodeni, 137 cases of ulcus ventriculi, 17 cases of ulcus ventriculi et duodeni, and 3 where the pathological diagnosis of perigastritis adhesiva (no ulcer being found) was obtained. In 27 cases the resection of exclusion was performed and in all others the ulcer bearing portion of stomach or duodenum was resected with the distal two-thirds of the stomach.

The pre-operative, operative, and postoperative treatment as given by Starlinger is identical with the treatment in the Eiselsberg clinic and does not require repetition here.

Anæsthesia has been predominantly by the open drop ether method, though local anæsthesia (splanchnic), spinal, and gas oxygen anæsthesia have been employed. There was no appreciable difference in mortality or morbidity though it must, of course, be taken into consideration that the cases for local anæsthesia represent a somewhat selected group where ether had been thought dangerous. The following table shows the distribution of cases.

TABLE I.—ANÆSTHESIA

	Cases
Ether (open drop method)	526
Nitrous oxide-oxygen	8
Spinal (spinocain)	18
Local (infiltration and splanchnic)	42
Local (infiltration and ether)	11
Billroth mixture	1

The most popular type of operation has been that modification of the Billroth Type II, in which the cut end of the remaining third or fourth of the stomach is united in its entirety with the jejunum retrocolically; the oral portion of the jejunum being sutured to the lesser curvature. Where conditions have been favorable the Billroth I, in the end-to-end, or end-to-side (supra or infrapapillary) modification has been employed. In those cases in which it was feared that excision of the ulcer bearing duodenum might injure the pancreas or biliary tracts, the Eiselsberg resection of exclusion was employed (*Resektion zur Auschaltung*). There was little or nothing to indicate any difference in mortality or morbidity according to the type of operation performed.

TABLE II.—OPERATIONS

	Cases
Billroth II with retrocolic gastrojejunostomy	528
Billroth II with antecolic gastrojejunostomy and entero-anastomosis	2
Billroth II (exclusion of pylorus)	27
Billroth I (usual gastroduodenostomy)	22
Billroth I (infrapapillary gastroduodenostomy)	27

The mortality for the entire series was 5.44 per cent. As might be expected, there is con-

[1] Ann. Surg., 1930, xcii.

[2] v. Haberer, H. Lehrbuch der Chirurgie A. von Eiselsberg gewidmet, Bd. I, 596. Julius Springer, 1930.

[3] Starlinger, F. Arch. f. klin. Chir., 1927, cxl.ii, No. 1, 8.

siderable variation in the mortality rate in perforated and non-perforated ulcer as well as in ulcus ventriculi as contrasted with ulcus duodeni.

TABLE III.—MORTALITY

		Per cent
Total resections	606	
Deaths	33	5.44
Ulcus duodeni (not perforated)	422	
Deaths	16	3.79
Ulcus duodeni (perforated)	27	
Deaths	3	11.1
Ulcus ventriculi (not perforated)	134	
Deaths	14	10.44
Ulcus ventriculi (perforated)	3	
Deaths	2	66.66
Ulcus ventriculi et duodeni	17	
Deaths	0	0.
Perigastritis adhesiva	3	
Deaths	0	0.

The most frequent causes of death were pneumonia and peritonitis in one or another combination. As the causal factor of peritonitis as determined by postmortem may be of interest, they are tabulated separately below:

TABLE IV.—CAUSES OF DEATH

	Cases
Pneumonia	8
Pneumonia and ileus	1
Pneumonia and peritonitis	6
Pneumonia, subphrenic abscess	1
Pneumonia, subphrenic abscess, and pleurisy	1
Peritonitis	14
Peritonitis and hæmorrhage	1
Subphrenic abscess	1

TABLE IVA.

Peritonitis—total	21
of unknown origin	11
Due to:	
a—Anastomosis suture line leakage	4
b—Duodenal stump leakage	2
c—Ileus (strangulated)	1
d—Perforated ulcers	3
e—Subphrenic abscess, leakage of anastomosis	2

The following cases presented features somewhat out of the ordinary and are here abstracted.

CASE 1. A patient, aged 44 years, was operated upon under local anæsthesia, for ulcus duodeni. An infrapapillary Billroth No. 1 was performed. On the sixth day after operation a laparotomy was again done because of severe pain in the epigastrium. In the anterior suture row of the anastomosis was found a small perforation which was closed over, and an anterior gastro-enterostomy with entero-anastomosis was performed. Death occurred 10 days after the second operation. At postmortem there was found pneumonia, purulent diffuse bronchitis with localized peritonitis.

CASE 2. A patient, aged 37 years, was operated upon under ether anæsthesia, for ulcus duodeni. An infrapapillary Billroth No. 1 was performed. There was much vomiting and on the eighth day after operation the abdomen was again opened up. At the second operation, a few drops of pus were found in the suture line of the duodenal stump and the duodenum at the anastomosis was covered over by the omentum. An anterior gastro-enterostomy with entero-anastomosis was performed and drainage was given to the duodenal stump. The second day after operation, intestinal contents appeared in the drainage opening. The wound was again opened and the opening in the duodenum sutured. The patient died 5 days after the third operation. Postmortem examination showed pneumonia, subphrenic abscess, and insufficiency of the suture lines in the duodenal stump and in the gastroduodenal anastomosis.

TABLE V.—COMMON COMPLICATIONS

	Cases
Pneumonia	14
Pneumonia and pleurisy	1
Pleurisy	4
Subphrenic abscess	2
Severe postoperative bleeding and vomiting (1)	4
Diarrhoea	5
Secondary suture (wound bursting open)	2
Thrombophlebitis	2
Infarct (pulmonary) transferred	2
Urinary retention (more than 1 day postoperative)	2

CASE 3. Patient, aged 28 years, had a Billroth No. 2 operation, done under ether anæsthesia, for ulcus duodeni. Patient complained continuously of pain after the operation and was again operated upon on the ninth day after the first operation, when a strangulated ileus was found. The efferent and afferent jejunal loops had been strangulated by the opening in the mesocolon. At postmortem examination general peritonitis was found.

CASE 4. A Billroth No. 2 operation was performed, under ether anæsthesia, upon a patient aged 53 years, who suffered from ulcus duodeni. Symptoms of peritonitis appeared and a second operation was done 2 days after the first. Small abscesses were found in every suture hole. At postmortem examination general peritonitis was found.

CASE 5. A Billroth No. 2 operation was performed upon a patient aged 42 years, for the relief of an ulcus ventriculi. The operation was done under ether anæsthesia. Signs of severe peritonitis appeared on the following day and necessitated a second laparotomy. Perforation was found at this time through part of the ulcer which had not been removed. General peritonitis was determined at postmortem.

CASE 6. A Billroth No. 2 operation was performed under ether anæsthesia upon a patient aged 45 years, who suffered from an ulcus ventriculi. Signs of stenosis appeared after the sixth day. On the tenth day laparotomy was again performed. The anastomosis was found adherent to the liver and was very œdematous. An anterior gastro-enterostomy with entero-anastomosis was performed. Death followed 4 days later. Lobar pneumonia was determined at postmortem examination.

Pneumonia plays a leading rôle again, this time as a factor complicating the postoperative course. The major complications observed are tabulated in Table V.

Those cases which presented unusual features are given in brief:

CASE 7. Under ether anæsthesia, a Billroth No. 2 operation was performed for ulcus ventriculi. Because of the appearance of symptoms of ileus, the abdomen was

again opened up and an entero-anastomosis was performed between the loops of the previous retrocolic anastomosis. The wound healed by granulation. The patient also developed severe bronchitis and pleurisy, but after 3 months in the hospital was discharged cured.

CASE 8. A patient, aged 24 years, had a duodenal ulcer for which an infrapapillary Billroth No. 1 was done. The patient vomited daily and 5 days after operation, because of his generally poor condition, he was operated upon again, an anterior gastro-enterostomy with entero-anastomosis being performed for security's sake. The patient made a complete and rapid recovery.

CASE 9. Under nitrous oxide oxygen anæsthesia, a Billroth No. 2 operation was done upon a patient aged 63 years, who was suffering from a duodenal ulcer. A pancreatic fistula appeared on the fourteenth day after operation, and this was not entirely healed when the patient was discharged from the hospital.

CASE 10. Under ether anæsthesia, a Billroth No. 2 operation was performed upon a patient 41 years of age, who was suffering from a duodenal ulcer. There was severe bleeding by mouth the afternoon of the operation and this condition was treated by means of lavage with 1:1000 silver nitrate solution and 2 intravenous injections of 1 cubic centimeter of afenil, without success. The abdomen was again opened and gastrotomy was performed. No spurting vessels were seen, but profuse bleeding from the anastomosis was observed. The entire anastomosis line was resutured with a running catgut suture, and the abdomen was closed. One and one-half liters of saline was given at the close of the operation. The following night the patient was very weak and was given a 500 cubic centimeter emergency blood transfusion. This was repeated again in 2 days. Patient was discharged cured.

CASE 11. A patient 39 years of age was operated upon under ether anæsthesia for duodenal ulcer. A Billroth No. 2 was done. A duodenal fistula appeared which was healed at the time of discharge.

CASE 12. An infrapapillary Billroth No. 1 was done upon a patient 29 years of age, who had a duodenal ulcer. Because of symptoms of stenosis the patient was operated upon again a week later. There was an angulation of the lowest duodenal angle caused by omental adhesions. The adhesions were separated and the abdomen was closed. A subphrenic abscess was suspected 23 days later but was not found. The patient was discharged cured.

SUMMARY

In a series totalling 606 partial gastrectomies for peptic ulcer in the Eiselsberg clinic there were 33 deaths, a mortality of 5.44 per cent; in those cases surviving—573 in number—60 presented some more or less serious complication in the postoperative course.

THE CONDUCT OF LABOR IN THE DYSTOCIA DYSTROPHIA SYNDROME PATIENT

EDWARD LYMAN CORNELL, M.D., F.A.C.S., CHICAGO

THE patient who presents a big problem for the obstetrician is the one at present most frequently overlooked by the general practitioner and the young obstetrician. She has been classed here under the term *dystocia dystrophia syndrome*. Most textbooks devote only a meager paragraph or two to the discussion of this type of case; in fact, unless one looks carefully through the index he fails to find any reference. Yet, my experience with this type of patient leads me to state that she presents many more problems in the management of her delivery than does the patient with a generally contracted or flat pelvis. This is chiefly because such cases are not recognized as pathological entities until too late, except by trained obstetricians.

To this syndrome, DeLee has applied the term dystocia dystrophia syndrome. Welz has used the term sporadic cretinism, while the term dystrophia adiposogenitalis has been rather loosely employed by other writers. The literature on the subject is limited. I have been able to find only a few references aside from those written by members of the Chicago Lying-In Hospital staff. Welz, Loizeaux, Solomons and Taylor, A. B. Davis, Horner, and Greenhill are among the few who have contributed to the subject. With the exception of the two latter, the remarks are confined to one or two paragraphs and nothing very definite is stated to guide the physician in the management of this difficult type of case during labor.

The term dystocia dystrophia syndrome is probably as good a term as it is possible to employ. In Stedman's dictionary the terms are defined as follows: "Dystocia, difficult childbirth. It is called fetal or maternal according as the cause is in some abnormality of the fetus or in uterine inertia or some obstruction in the parturient canal." Dystrophia is defined as defective nutrition, while syndrome means the aggregate of symptoms associated with any morbid process, and constituting together the picture of the disease. I have not been able to find any term which better describes this type of patient than the one DeLee has given.

The dystocia dystrophia syndrome is not confined to any particular race. I have seen cases in the white race of most nationalities with the possible exception of those of Southern Europe, and a number of cases in the colored race, although here it is quite rare. Social status seems to bear no relation to the condition, as it is found in private practice as well as in the charity clinics. It is not unusual to find the girls in the family of a similar type. On the other hand, the patient may be an only child.

These patients not infrequently give a history of irregular menstruation. They may miss their periods for as long as a year or they may menstruate only three or four times a year. Dysmenorrhœa is a common complaint. During married life there is a tendency toward varying degrees of sterility. It seems to be difficult for such a patient to become pregnant and yet on examination little or no pathology is found in the pelvis. In some patients quite the reverse is true, and I have had a few in whom there was no difficulty whatever either in menstruation or as to fecundity. Many complain of difficulties in sex life, i.e., absence of libido, vaginismus, etc.

These patients present a rather striking appearance. They are short and abnormally stout; their height is usually around 5 feet and the weight varies from 150 pounds for the shorter group to 200 pounds for the taller. Face and cheeks are fat and neck short, all of which give the head a squatty appearance. The chest is broad, the arms short and fat, the abdomen plump with more or less of a fat apron, and the hips and legs well padded and heavy. The hips particularly attract the attention of the physician because they are so broad. On closer inspection of the extremities it is to be noted that the humerus and femur are not out of proportion, but the other bones, both the long and short ones of the hands and feet, are shortened considerably. The hands present a stubby appearance where the second, third, and fourth fingers are more or less of the same length, and especially is this noticeable with the first and third fingers. It resembles a spade hand. The foot is short and presents a squatty appearance; the toes are short and fat. The wrists and ankles are heavy and thick. The measurement of the elbow to the wrist, i.e., from the olecranon to the os lunatum is about 23 centimeters, whereas in the average woman this measurement is 25 centimeters plus. All the bones are thicker and appear harder than do those in the average woman.

The pelvis usually presents little that is abnormal except that the bones are thicker. The external measurements are usually normal or above normal. In the latter case they may vary as much as 1 centimeter for each of the pelvic measurements. The Baudelocque diameter is usually about 20 to 21, although, as in Case 1, it has been found to be larger due to the fat pad. One notices that it is somewhat difficult to outline the pelvic bones externally because of the firmness of the muscle structure and the amount of fat present. On internal examination the vagina may be short and present a sense of fullness as it is well padded with fat. These patients are usually highly sensitive to vaginal examination and it is rather difficult in many of them, especially in the high grade type, to outline the various structures of the pelvis with any degree of certainty. In a few of these patients before pregnancy I have noted that the uterus seems to be smaller than normal, although it is not what we might term an infantile uterus. The pubic rami are greatly thickened; the perineum and the vaginal walls seem to lack the same degree of elasticity that is usually noted in the normal patient.

The skin is usually pale in color, even in the negro race, and in a few instances it has presented a pasty appearance such as one would expect to find with kidney disease. The blood count is seldom much below normal, although as a rule, the hæmoglobin is slightly below 80 per cent. Occasionally the hair markings are similar to that found in the male, although this is not necessarily a distinctive feature. On most of these women, however, there is considerable hair on the lower abdomen and a profusion on the escutcheon.

During pregnancy these women have many complaints, which are minor in character, but it requires considerable tact on the part of the attending physician to keep up their morale. Spotting in the first trimester is not uncommon. Abortions occur easily and somewhat more frequently than in the usual run of patients. They gain rapidly in weight, often as much as 10 pounds a month in spite of dietary measures to control the gain.

These women are prone to toxæmia of pregnancy, especially in the ninth month, and they not infrequently quickly develop eclampsia or eclampsism. They nearly all go over term, often as much as 2 weeks or more. They have large babies, and it is to be noted that the baby's bones are harder than those of the average.

With the onset of labor, things do not start out correctly. As one of my residents told me several years ago, "they go into labor on the wrong foot." Usually the bag of waters ruptures before the onset of pain, anywhere from a few hours to several days. When the contractions start they are very painful to the patient, but they are not strong to the palpating hand. The interval between contractions is irregular and may remain so for many hours. The administration of quinine with or without castor oil not infrequently increases the painfulness of the contraction but does not affect its intensity, so far as cervical dilatation is concerned. It seldom causes the pains to become regular. The morale of the patient is easily broken and she cries out bitterly with each contraction, and unless one is familiar with this type of patient he is inclined to believe that he is dealing with a hysterical woman. This is quite to the contrary. These women do have considerable pain. It seems to me that they are hypersensitive and that we should not consider them as cases of hysteria in labor but should pity them because of their inability to withstand pain.

The baby presents in a cephalic posterior position with somewhat more than the usual amount of deflection. It remains thus throughout the labor or at best rotates to the transverse position. An anterior position is so rare that I cannot recall seeing one in the past 5 years.

The progress of labor is exceedingly slow and tedious. For the number of contractions that they have, at least two other women and sometimes many more would be delivered. Not infrequently at the end of 24 hours of more or less active labor, there is only 2 to 3 centimeters' dilatation. Formerly, it was my practice to use oxytocic drugs to stimulate the labor pains, but I found that such medication merely increased the amount of pain without producing an appreciable amount of dilatation. The introduction of bags will secure dilatation up to 9 or 10 centimeters, but the amount of suffering that these patients have with the bag in place in spite of the use of morphin and other analgesics is almost beyond mention.

Delivery from below has been accomplished by means of Duehrssen's incisions with rotation of the head, usually from the transverse position, and the application of mid forceps with a deep episiotomy and the extension of this episiotomy upward 2 or more centimeters. The baby is large and its head not infrequently badly marked with the forceps, occasionally the blades cutting through the scalp. The baby is asphyxiated and needs considerable resuscitation or it may die during the course of its delivery or shortly thereafter from brain hæmorrhage.

If an episiotomy has not been done the mother is badly lacerated, the cervix is badly torn, thus inviting sepsis, which appears very readily in these patients.

A. B. Davis has very aptly said of these patients, "In many of them if the pelvic delivery, dilatation, and incisions of the cervix and forceps are persisted in, the operator does not usually look upon his completed work with pride. If version is attempted, too often the results are not good. Many of them become unsafe for classical cæsarean section, unless it is done early, because of the reason of sepsis. This type of case gives the high percentage of stillbirths, cerebral hæmorrhages, broken necks, children in whom the heart continues to beat for an hour more or less, and then it is impossible to start respirations, or those who die soon after birth."

The difficulty in forceps delivery does not come at the outlet of the pelvis but more often at the inlet or the midplane because the soft structures of the pelvis lack elasticity. Thus we obtain these bad lacerations.

In the borderline case of this type spontaneous delivery is rare. However, these borderline patients not infrequently go into labor promptly and continue to complete dilatation and then progress stops. It becomes necessary to deliver them by low or mid forceps, and even then it is surprising how much damage is done to the pelvic floor and vaginal canal.

It is very unwise to attempt the induction of labor in these patients, irrespective of the method employed. It is my opinion that it is impossible to tell in advance whether or not these patients will go into labor promptly, will continue in labor, and will give the obstetrician a reasonable chance to deliver them from below. Even with a rather extensive experience, I am unable to answer these questions. A few patients for whom I have predicted a tedious labor have delivered rather promptly while those in whom a prompt delivery was forecast have given considerable trouble.

Breech presentation is the *bête noir* in this class of patients. Fortunately, I have had only a few. External version before labor is almost impossible because of the excess of fat on the abdomen. In fact, breech presentation is seldom diagnosed until the patient is in labor. To induce labor in these patients is to court disaster with a vengeance. I always do a cæsarean section on these women if they are near 35 years of age, regardless of the degree of the dystocia dystrophia syndrome.

The ideal management of the dystocia dystrophia syndrome patient consists in placing her in the hospital when she goes into labor and never inducing labor by mechanical means even in the presence of toxæmia of pregnancy. While it is true that an occasional case comes through nicely on mechanical induction, it is so infrequent as to be negligible. When the patient enters the hospital in labor everything possible should be done to keep up her morale while giving her a test of labor. My procedure consists usually in the use of morphin, ¼ grain, as soon as the patient presents evidence of becoming tired, not when she is exhausted. This is followed by a rectal instillation of ether and quinine, 10 grains, as recommended by Gwathmey. If the patient does not progress after 18 to 24 hours of labor with relatively good contractions I have resorted almost invariably to the low cervical cæsarean section. During the progress of the trial labor, I have been cautious in the number of rectal examinations. No vaginal examinations are made. One must watch these patients carefully for the appearance of Bandl's ring, tetany, or a thinning out of the lower uterine segment. On the appearance of any of these signs labor should be terminated. If the patient presents a moderate or severe grade of toxæmia of pregnancy, it is advisable to terminate labor by cæsarean section, provided the child is viable. It is understood, of course, that the proper medical treatment for the toxæmia has not been successful. Cases with eclampsia do not do well under the Stroganoff treatment, because the labor factor is still present and cannot be overcome.

I do not feel that this is an abuse of cæsarean section, and I heartily agree with A. B. Davis who says, "would it not be better to foresee some of this and abuse cæsarean section in more of these cases and do it early when it is comparatively safe for mother and child?"

In the borderline patient, young in years, I give a test of labor, provided I believe the baby to weigh 8 to 8½ pounds. If progress is not satisfactory, then I perform a cæsarean section.

After having witnessed the stormy recovery, and after listening to the complaints of these women for several months after delivery on several occasions, I must confess that I would rather decline to handle these cases if I could not resort to cæsarean section in cases in which labor is not normal.

If the woman goes into premature labor, or if the baby should be small for any reason, the labor may approach normal. Usually, however, the first stage is protracted, but the patient not infrequently delivers spontaneously or with low forceps. Other factors being equal, I always give them a long test of labor.

The suggestions made for primiparæ do not hold if any of these patients has delivered by a difficult forceps with lacerations. The subsequent labors are frequently comparatively rapid and spontaneous because vaginal resistance is gone.

I will cite just a few cases to demonstrate the course in these instances. The cases are not selected by any means; they are the usual run in obstetrics. Merely the essential details are noted.

CASE 1. Mrs. K., No. 77203, aged 34 years, first reported October 31, 1929. She had been married 1 year. Last menstrual period was August 7, 1929. She was 64 inches tall in shoes and weighed 208 pounds with clothing. Blood pressure was 152-80. Urine was negative. Pelvic measurements 28.5, 31, 36, 25, and diagonal conjugate 12. It was noted that she was a typical dystocia dystrophia syndrome.

She entered the hospital January 9, 1930, with much œdema and a systolic blood pressure of 160. On rest in bed she improved and was sent home on January 13, with blood pressure 148-100. On March 3 she showed 1+ albumin. Thereafter until March 21 the urine was the same and the highest blood pressure 156-110. On March 21 the urine showed 2+ albumin and hyaline casts. She re-entered the hospital March 20 because the bag of waters had ruptured at 8:30 a.m. She had irregular pains all that day. On the morning of the 21st she was given castor oil and quinine which did not increase the pain or regularity. Blood pressure was gradually climbing until it reached 178-108. At 4:30 p.m. a 5 centimeter bag was inserted. This was expelled at 9:45 p.m. The pains were strong, at 3 minute intervals. She had strong pains all night. At 6:15 a.m., March 22, a 9 centimeter bag was inserted, at which time the cervix was still thick. She was given morphin, ¼ grain, for rest. The bag came out at 9 a.m. The blood pressure was still high. Pains were irregular and alternately strong and weak. They remained that way all night. No progress was made all the next morning. As the patient's pulse rate was increasing and she was becoming exhausted delivery was done, according to the following technique: Cervix thick; 8 centimeters Duehrssen's incisions; occiput left posterior; manual rotation to occiput left transverse; application of forceps and further rotation; then strong traction with the delivery of a 2,775 gram boy. The head was much molded with a large caput. The perineum was saved by a deep left mediolateral episiotomy but the vagina had a deep extension above the episiotomy wound. The entire delivery took 1½ hours. Blood pressure was 152-110. The mother made a good recovery, the highest temperature being 100 degrees on 3 consecutive days. She left the hospital with a blood pressure of 138-100 and 1+ albumin in the urine. The time from the rupture of the bag of waters until delivery was 79 hours.

Here, then, is a patient who went into labor at the beginning of the eighth month, with a small baby, and had a very tedious time. It demonstrates clearly that drugs and mechanical means of inducing dilation of the cervix do not work satisfactorily in these patients. One hesitates to do a cæsarean section on a premature baby, but certainly the wear and tear on both the physician and patient would justify it occasionally. It will be noted that this woman was 34 years old. The Baudelocque diameter was 25. This is unusually large but it was due to the pad of fat over the sacrum and pubis.

The staff man in charge of this patient stated after delivery that had he known the difficulties to be overcome, he would have done a cæsarean section at the time he decided to insert the first bag. In this I would agree.

CASE 2. Mrs. L., private patient No. 2590, aged 23 years, reported August 1, 1929. She had been married 5 years and in spite of many attempts had never become pregnant. Her height was 61 inches and weight 128 pounds, both taken with clothes on. Her last menstrual period was April 14, 1929. General examination was negative. Pelvic measures were spinous 24½; intercristal 28½; transverse 32; Baudelocque 19½; diagonal conjugate 12. Blood pressure was 126-80.

On September 15, she entered the hospital with signs of a threatened abortion, diagnosed from occasional pain with bloody vaginal discharge. Rest in bed cleared this up and she went home in a few days. On October 28, she reported with thrush of the vagina which resisted treatment until January 9, 1930, when it was cured. At this visit she complained severely of an itching dermatosis which was diagnosed as a toxic rash due to pregnancy. She had gained much in weight, now 172 pounds. Blood pressure was 130-90. The rash resisted all lines of treatment suggested by myself and a dermatologist.

From the menstrual date we estimated that she was due January 21. She felt the baby September 7 and would be due February 8. She began labor February 1, 1930, at 12:01 a.m., with pain. The pains were weak and at 10 minute intervals. Quinine, 5 grains, was given at 9 a.m. At this time there was no dilatation and only partial effacement of the cervix. The head was not engaged, although fixed. The position was occiput left posterior. At midnight the cervix was dilated 3 centimeters and the pains were moderate, coming every 3 to 4 minutes. At this time morphin sulphate, ¼ grain, and 2 cubic centimeters of 50 per cent magnesium sulphate were given hypodermically, followed by the Gwathmey rectal instillation. Patient had some rest and at 10 a.m. the following morning she had 3 centimeters' dilatation after having had strong pains every 2 to 3 minutes for 5 hours. She was beginning to show signs of exhaustion, so a laparotrachelotomy was done under local anæsthesia, one-half per cent novocain being used. The operation was easily accomplished; a baby boy was born weighing 4,220 grams.

This patient was in labor for 35¼ hours. She made a prompt recovery, the highest temperature being 100 degrees on the second day. No complications were encountered.

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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NOVEMBER, 1931

ART AND PERSONALITY IN SURGERY

IN speaking of art, it is not my purpose to confuse it with handicraft in surgery. Surgeons have gone about as far as possible in this respect. Advancement must be made in other lines. When my assistantship to a great surgeon was finished, he gave me this parting admonition: "Seventy-five per cent of your ultimate success in life will depend upon your ability to handle people, twenty-five per cent on your knowledge of medicine. Try to excel in both." Reduced to its simplest terms, art and personality in the practice of surgery consists of the ability to understand and deal with people as human beings, and not alone with their diseases.

Recently there has been much discussion of a feeling of dissatisfaction among physicians and patients. The paths of thought of physicians and laymen, especially the more informed laymen, have diverged; they are no longer thinking along the same lines. Among other things, patients are seeking relief, and we, as physicians, are seeking information. This rift, being not only intellectual but temperamental, tends to prevent that human understanding so necessary to a complete evaluation of the patient, and that human touch which is so essential if we are to be healers of the diseased body and mind, and not mere craftsmen employed to repair an injured organ or to remove infected tissue.

This state of affairs is probably due to our critical and analytical manner of thinking. Each man in the profession has cut out for himself a segment from biology and is working therein with astonishing industry and acuteness of intellect, without regard for a visualization of the subject as a whole. The physician of today who thinks only anatomically, chemically, or physiologically cannot understand the patient before him. He is unable to perceive the manifest symptoms in their proper relationship or to recognize all the forces at work to injure or to benefit the patient. In this analytic age, it is almost impossible even to apprehend the spirit in which the great physician Hufeland said, "Every patient is a temple of nature. Approach him with reverence." It seems that our artistic or synthetic capacities have not kept pace with our analytic activities. In this endless chain of disintegrating effort, we have all but lost sight of the fact that originally there must have been something to bind the parts of man together.

An artist may be described as one who is able to build up from scattered fragments a recognizable unity. In the field of medicine and surgery, this unity, this completed work of art, may be a satisfactory diagnosis, an adequate plan of treatment, a rehabilitated patient.

Let us now turn to personality. It is difficult to analyze this quality. We might say that it consists of character, intellect, will, and feeling, with a physical vehicle having peculiarities of its own. These factors, however, will remain inert until there has been added that something which quite defies definition: the power to make an impression upon the soul of another.

What is this soul so susceptible to the power of personality? I would call it the unifying principle of the organism, that invisible presence, the agitation of which may be noted in every system of the body. When it is perturbed, the muscles become tense, the eyes sparkle, respiration and heart action quicken, the face flushes, and the entire body response is evident.

When and how is the surgeon to use his personality as a therapeutic agent? He should use it without interruption from the patient's first visit to the time when he is fully prepared, mentally as well as physically, to return to normal life. As he zealously guards against unnecessary trauma to the tissues, he should, in like manner, safeguard the patient's psyche in the consulting room. At that moment the soul lies open and exposed to injury from incautious comment dropped by the surgeon or his assistants. It is already traumatized by the suspense and fear incident to the visit. The wise physician will immediately assuage this unhappy condition and protect the patient from further disturbance by the therapeutic power of his personality.

We cannot excuse ourselves by saying we have nothing to do with the patient's mind, that we are not psychiatrists but surgeons, and have agreed to look only after his body. The matter is not so simple. The physical and the psychical are so interwoven that no one can say, "Here the physical ends; there the psychical begins."

The physician or surgeon must carry the patient on through all those events which transpire from the first visit to the final consummation of the whole transaction. "The operation, although the most dramatic, is but one incident," said Moynihan. The postoperative course may be interrupted by unforeseen complications. Suffering often wears heavily on the patient; long days and sleepless nights play havoc with his reserve nerve force. He needs all the help that can be afforded him at such a time. Herein lies the opportunity for the surgeon to apply his power of personality to the greatest advantage. Such a personal influence must be a constant encouragement, never ceasing until the victory is won and the patient is returned again to his family and his business.

The surgeon who serves best and profits most is he who has been able to include in his training that artistic element of understanding which permits him to separate the essentials from the non-essentials, and who has developed and guided a hopeful and pleasing personality to the beneficent end that his patients may be restored to health.

R. L. SANDERS.

TREATMENT OF ACUTE CRANIOCEREBRAL INJURIES

IN the treatment of acute craniocerebral injuries one is concerned with the injury to the brain. Therapeusis as regards cranial injuries is indicated only when the lesion is a compound or depressed fracture. A fracture of the skull *per se* unless of one of the two mentioned types may be totally disregarded in the treatment of acute craniocerebral injuries. Within the past decade the treatment of acute craniocerebral injuries has become largely that of conservatism. Prior to this time the operative treatment was employed in from 20 to 30 per cent of all cases,

whereas at the present time probably less than 5 per cent of all cases of acute craniocerebral injury are subjected to operative intervention. It is now generally accepted that conservative treatment is not only less dangerous, but also more efficacious than the operative treatment in the majority of cases of craniocerebral injury, at least in those cases with no localizing signs. The conservative treatment of craniocerebral injuries is largely dependent upon the comparatively recently appreciated fact that the most frequent cerebral lesion subsequent to a head trauma is an œdema of the brain substance. As shown by the pioneer work of Weed and McKibben, cerebral œdema can be very effectively treated by the intravenous introduction of hypertonic solutions, and upon this fact is based the modern treatment of acute craniocerebral injuries.

As in all other major traumas, acute craniocerebral injuries are frequently associated with surgical shock, and it is, therefore, of utmost importance that shock should first be treated. The usual methods, such as lowering the head, the application of heat to the body, and intravenous infusions should be used. Ideally, as advocated by Fay and Thomas, hypertonic (50 per cent) glucose solution should be used for the infusion. Fay has rightfully warned against the use of magnesium sulphate during the period of shock, in that further dehydration of the body is undesirable.

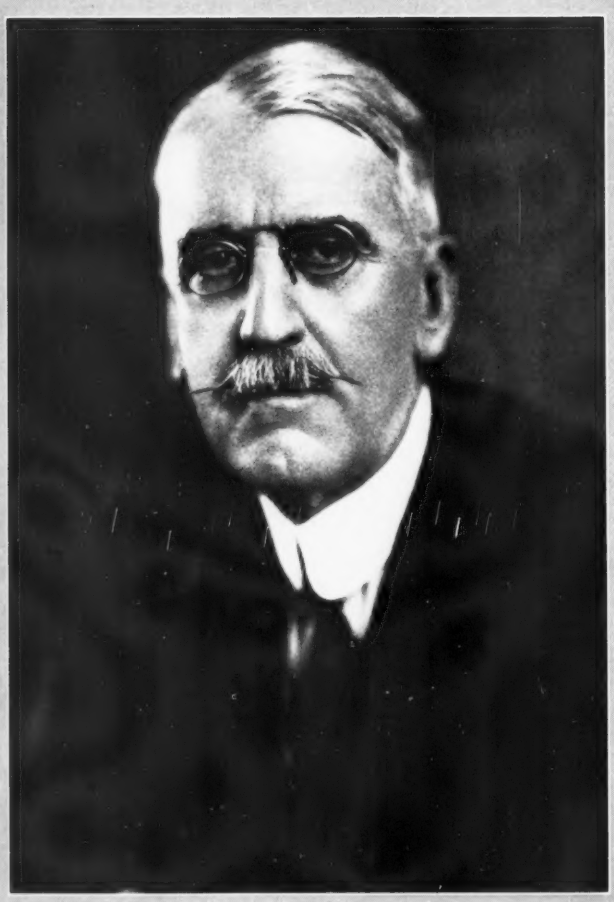
The treatment of a case of acute craniocerebral injury without a knowledge of the cerebrospinal fluid pressure is more or less haphazard. Every patient with a major head injury should be given the advantage of lumbar puncture with the manometric determination of the cerebrospinal fluid pressure. In those cases in which there is a cerebrospinal fluid hypertension it is advisable to relieve the increase in pressure by slowly and cautiously removing some of the cerebrospinal fluid. This can be accomplished safely by the gradual escape of enough cerebrospinal fluid to reduce excessive pressure above 10 millimeters of mercury by one-half, i.e., if the cerebrospinal fluid pressure is 20 millimeters of mercury, enough fluid should be withdrawn to reduce the pressure to 15 millimeters of mercury. Lumbar drainage is especially indicated in those cases in which blood is present in the cerebrospinal fluid, as has been shown by the researches of Bagley.

As mentioned above, the increased intracranial tension due to cerebral œdema is best controlled by the use of hypertonic solutions. The intravenous injection of hypertonic solutions, especially 50 per cent glucose, is most efficacious. Hypertonic solutions of sodium chloride as first advocated by Weed and McKibben should not be used, because sodium chloride being a dialyzable salt is absorbed and leads to secondary tissue retention with a rapid return of symptoms due to an increased œdema. The administration of magnesium sulphate either by mouth or by rectum is to be highly recommended. Fay has demonstrated that magnesium sulphate is about twice as efficient as sodium chloride when used as a dehydrating agent in the intestines. In the dehydration therapy, it is essential that the fluid intake must be limited and probably should not exceed 500 to 600 cubic centimeters in 24 hours. It is important, however, that "over dehydration" should be prevented. Leriche, in 1920, emphasized that relatively infrequently in acute craniocerebral injuries there may be an associated hypotension of the cerebrospinal fluid pressure rather than a hypertension. In such cases Leriche and others have advocated and have successfully employed intravenous injections of sterile distilled water or of hypotonic solutions.

The operative treatment of craniocerebral

injuries is indicated in a relatively small number of cases which may be grouped as follows: (1) scalp wounds; (2) compound fractures; (3) localized hæmatoma, especially from the middle meningeal artery; and (4) occasionally in depressed fractures of the skull. In the first two groups, i.e., scalp wounds and compound fractures, thorough débridement followed by primary suture should be done. In the second group, craniotomy with evacuation of the blood clot is indicated; and in the third group in which there is pressure on the cerebral substance, elevation of the depressed fragments should be performed. The operative treatment of acute craniocerebral injuries occupies a relatively small part of the treatment, and it should be stressed that the conservative treatment, especially the use of hypertonic solutions, both intravenously by way of the alimentary tract, as well as repeated lumbar taps, are the methods of choice.

ALTON OCHSNER.



MEMOIRS

JOHN BLAIR DEAVER

Born July 25, 1855—Died September 25, 1931

IN the death of John Blair Deaver the medical and surgical world, and thousands of grateful patients throughout the land mourn the loss of a master surgeon. I doubt if the passing of any surgeon of our time has created a greater void and deeper regret.

This enthusiastic statesman of surgery was a star operator, and early achieved international fame. He loved his chosen work which he pursued, with great industry and without signs of weakening, to the age of seventy-five. The surgeons of every land, when they visit Philadelphia in the future, will miss this genial host with his philosophy, his irrepressible humor, his diagnostic skill, and his marvelous technique.

The American College of Surgeons and its official journal—SURGERY, GYNECOLOGY AND OBSTETRICS—have lost a great friend. Dr. Deaver was a Founder of the College, a member of its Board of Governors since 1913, a Regent and President, 1921 to 1922. He was a generous contributor to the journal. Among his last contributions to surgical literature is his article on "The Common Bile Duct" which appears elsewhere in this issue of the journal. Like all great men, he was never too busy to do a thing that was worth while, and it is typical of the man that within thirty-six hours of his death he was busy correcting and editing papers which he planned to present before medical groups.

Though he has departed from our midst, there are hundreds of active surgeons who were his students and whose skill commemorates the teachings of Deaver; and from his publications future generations of surgeons will gain practical knowledge and inspiration for all time to come. FRANKLIN H. MARTIN.

JOHN BLAIR DEAVER was born near Buck, Lancaster County, Pennsylvania, on July 25, 1855. His father, Joshua Montgomery Deaver, was a famous country doctor of Lancaster County. Dr. Deaver is survived by his widow, Caroline Randall Deaver; a son, Dr. J. Montgomery Deaver; and two daughters, Mrs. George G. Thomson (Elizabeth Deaver) and Mrs. Emory G. Alexander (Harriet Deaver). Dr. Harry Clay Deaver, a brother, also a surgeon of renown in Philadelphia, died June 25, 1931.

Doctor Deaver received his early education at the Nottingham Academy, near his childhood home, and was graduated from the University of Pennsylvania Medical School in 1878. He was resident physician in Germantown Hospital, and for an additional year served as interne at the Children's Hospital; entered the active practice of medicine in 1880, with offices at 16th and Vine Streets.

Philadelphia. Shortly thereafter he was appointed assistant demonstrator of anatomy in the University of Pennsylvania, which title he held until 1883; demonstrator of anatomy, 1884 to 1887; demonstrator of anatomy and lecturer on topographical anatomy, 1887 to 1891; assistant professor of applied anatomy, 1891 to 1899; professor of the practice of surgery, 1911 to 1918; John Rhea Barton professor of surgery, 1918 to 1922. (Because of his wonderful skill and popularity, the retirement age of sixty-five years for professors at the University of Pennsylvania was extended for one year in Doctor Deaver's behalf.) John Rhea Barton emeritus professor of surgery, 1922 until his death on September 25, 1931.

In March, 1918, Doctor Deaver was appointed professor of surgery in the Graduate School of Medicine of the University of Pennsylvania, and in July, 1931, he became emeritus professor of surgery. From 1886 until his death, Doctor Deaver was chief surgeon of the Lankenau Hospital.

Doctor Deaver was a member of the American College of Surgeons, American Surgical Association, American Medical Association, Interstate Postgraduate Medical Association of North America, Southern Surgical and Gynecological Society, Philadelphia County Medical Society, Medical Club of Philadelphia, College of Physicians and Surgeons of Philadelphia, Philadelphia Academy of Surgery, Philadelphia Obstetrical Society, Northern Medical Association of Philadelphia, and the J. Aitken Meigs Medical Association.

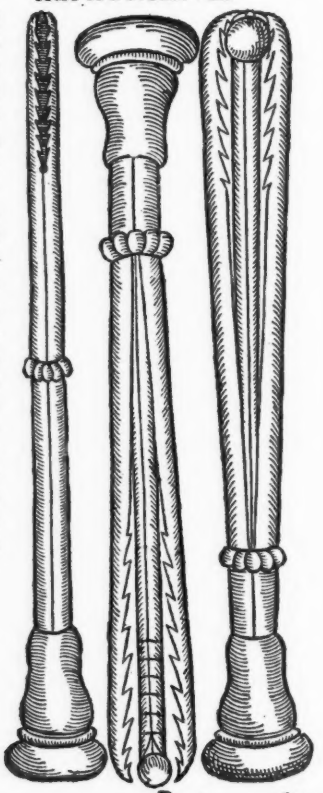
The John B. Deaver Surgical Society, an honorary organization in the Medical School of the University of Pennsylvania, is comprised of students who are particularly interested and adept in surgery. This society is unique in that it is probably the only one that has continued after the person for whom it was named ceased his active connection with the University.

Among the books of which Doctor Deaver was the author are: *Appendicitis; The Breast: Its Anomalies, Its Diseases and Their Treatment; Surgery of the Upper Abdomen* (1st and 2nd editions); *Enlargement of the Prostate, Its History, Anatomy, Æteology, Pathology, Clinical Causes, Symptoms, Diagnosis, Prognosis, Treatment, Technique of Operations and After Treatment* (1st and 2nd editions); *Surgical Anatomy of the Human Body* (three volumes); *Excursions into Surgical Subjects* (collected papers).

The list of articles which he contributed to medical journals totals 248, many of which have appeared from time to time in SURGERY, GYNECOLOGY AND OBSTETRICS.

ALPHONSINVM.

NOn inuoluendũ tamen filentio eſt gruinum roſtrum (vt vocant) vtpote quod & ipſum ad extrahẽdum inſtrumentum eſt excellentiſſimum, atque ab omnibus tũ veteribus, tum recentioribus cõmendatum: quo non ſolum pilulæ è difficillimis locis, ſed & alia, vt armorum, vt cæterarum rerum fruſtula extrahũtur. Huic nos, vt commodius manu ac valẽtius teneri poſſit, atq; ita pilæ, ac cætera extranea in vulnere certiùs explorari, annulos forpicularum modo adijcimus hoc pacto.



THE SURGEON'S LIBRARY

OLD MASTERPIECES IN SURGERY

ALFRED BROWN, M.D., F.A.C.S., OMAHA

ALPHONSO FERRI—CONCERNING THE TREATMENT OF GUNSHOT WOUNDS

LACK of knowledge of the details of a man's life sometimes makes it difficult to learn important things that should be known if one is to understand how to fit facts together and get at the fundamental reasons for events. The case of Alphonso Ferri is one in which this is exemplified almost perfectly. He is known as a personal physician to a Pope, Paul III, and so far as is known spent most of his life teaching surgery in Naples and Rome. This would make him a surgeon of civil life but he wrote one of the best books on the surgery of gunshot wounds of the period. He says in the introduction to his book that he is going to describe "the cures and remedies which we know to be the best after much study, the greatest diligence, and long use both at home and in war." This makes one believe he must have been a war surgeon. In another place, when writing of gunpowder, he states that he had the opportunity to study its effects in Hungary and Campania and at the siege of Landrecies when, in 1543, Charles V captured it from the French. That, of course, places him in the army in 1543 but in what capacity he does not say, nor does he or any record give us other data concerning his war record. We must, then, be satisfied in knowing that Ferri, though a physician to the Pope and his court, was at times a war surgeon.

Ferri was born at Faenza or Naples about 1500. Where he gained his early knowledge of surgery he does not tell us, and the first known of him is that he was teaching surgery in Naples when he was called to Rome by Paul III to become his physician in ordinary. During some of his years in Rome he taught surgery and specialized in it to a great extent except that he wrote two books besides his book on wounds, one having to do with the medicinal value of the sacred wood (Guaiac) and the other with the caruncles or calluses which arise in the neck of the bladder. In both these subjects he might have obtained considerable experience in his practice among the nobles at the papal court.

Much of Ferri's advice concerning the treatment of wounds coincides with that of the ancient authors. He quotes Hippocrates, Galen, and Celsus of the ancient schools and the major Arabists such as Rhazes, Avicenna, Albucasis, and others. He believes that gunshot wounds are all poisoned by the missile and advises removal of the bullet, for which purpose he has devised a forceps which he calls the "Alphonsinum." His canons or rules do not differ very much from present day teaching.

1. To seek for and draw out the lead ball and whatever has been carried in with it.
2. To manipulate the instrument that the drawing out may be most easily accomplished.
3. To destroy the poison with special medicaments.
4. To combat the crushing so that through it corruption of the part will not be hastened.
5. To remove completely all loose pieces of bone.
6. To replace the remaining pieces of bone in proper relation to the muscles and tendons so that the extremity can lay quiet.
7. To prevent suppuration.
8. To treat the wound with greatest care in all its stages so that evil chance may not befall.

Ferri advises searching the wound with the finger or sound to locate the projectile and loose pieces of bone if the wound is large enough. If it is small and sinuous, he uses various types of flexible probes or sounds and then uses his "Alphonsinum" to draw out foreign bodies. For his dressings he uses all kinds of medicines, following the usual ideas of the time. The search for the ideal wound antiseptic and healer was then going on, and each expert differed with the other. Ferri rather withdraws from the controversy by mentioning nearly everything and playing practically no favorites.

For hæmorrhage Ferri advises first the use of various styptic and clotting agents. If these do not work he then packs the wound with tampons covered with various medicaments and, only if this fails, does he stitch the vessel, using a long needle curved at the end which carries a thread through the eye at its base which is placed around the vessel and the vessel ligated. If the wound suppurates Ferri advises the use of drainage tubes.

Ferri's book on the caruncle or callus of the neck of the bladder which is printed with the 1583 edition of his book on wounds is extremely interesting. Reading between the lines he comes very near describing many of the growths of the bladder including enlargement of the prostate. A quotation will suffice to give the idea. He describes the caruncle as occurring in the following forms. "Simple, soft, hard, fungous, with a heavy white covering, warty, porous." Ferri deserves the title of the first to describe bladder pathology.

REVIEWS OF NEW BOOKS

NO condition in surgery is more perplexing in its diagnostic analysis or more difficult in its management than obstructive jaundice. Many problems are encountered by virtue of complicating physiological and anatomical anomalies. Walters in a brief monograph[1] endeavors to clarify some of these problems. His conclusions are drawn from experimental work and from a study of 514 cases of obstructive jaundice during a period of 8 years.

The author advocates the use of calcium chloride—5 cubic centimeters of a 10 per cent solution given intravenously on 3 successive days—in the preoperative preparation of the jaundiced patient. He believes that this procedure materially reduces the bleeding time and the tendency to hæmorrhage and that there are no toxic effects. He has also shown experimentally that in the presence of jaundice the lethal dose of calcium chloride is greater than in the absence of jaundice and that "following continuous injections of calcium chloride including therapeutic doses in normal and jaundiced dogs, no evidence of toxic effect on the kidney could be demonstrated, clinically or microscopically."

Since uræmia and hepatic insufficiency along with hæmorrhage, are the cause of death in obstructive jaundice, they are discussed in some detail.

It is shown that in the presence of obstruction of the extrahepatic ducts, marked changes occur in the intrahepatic ducts and liver structures, also that inflammation most likely plays a rôle in the production of stricture of the ducts. The author stresses the fact that "the successful treatment of stricture of the common bile duct and the hepatic duct is dependent on the fact that sufficient duct remains proximal to the stricture to permit an accurate anastomosis to an opening in the duodenum as well as that a minimal amount of infection exists in the walls of the ducts and the intrahepatic biliary passages."

This little work of approximately 130 pages affords the reader concise and practical information on the physiological and surgical aspects of obstructive jaundice. J. A. WOLFER.

OSTEOSYNTHESIS[2] may really be defined as the effort to apply internal splints to fractures. In order to cover all forms of open operation upon such lesions those procedures which do not involve the use of implanted foreign material of any kind must necessarily be included in statistical and other studies of the subject. Cornioley attempts to place in one volume a brief historical, biological, and practical review of the subject of internal splinting of fractures. The author's experience in 10 years' association with the office of the Swiss National Accident Insurance Administration has given him an opportunity to view end-results in a fair series of cases. KELLOGG SPEED.

IN the first portion of his book[3] Koenig discusses osteosynthesis in general. The anatomical findings, indications, aseptic technique, kind of anæsthesia, and operative procedure are given in detail.

The methods of artificial fixation of the fractured bones by suture, peg, plate, and screws are described. There is a chapter on the operative treatment and postoperative care of compound fractures. The second part of the book deals with osteosynthesis of various bones.

The book is well illustrated with numerous radiographs, photographs, and drawings. The author adds to our knowledge of the biological processes in fractures, through his studies and results obtained from operative surgical treatment. PHILIP LEWIN.

THE authors of *The Renal Lesion in Bright's Disease*[4] state that their purpose in presenting this work is identical with that of Volhard and Fahr in their *Die Brightsche Niernkrankheit* and they emphasize their study of the correlation of the renal lesion and the findings in the urine. The problem of classification and its discussion is somewhat avoided by the authors. Dr. Addis, by studying the changes in the urinary sediment has been able to choose by quantitative methods significant characteristics from among qualitatively similar processes and so has established a classification. Of course this is the whole point of Dr. Addis' careful studies of renal disease. The authors make the very important point that even though we understood normal kidney function, we would still be far from knowing the function of this greatly altered organ seen in Bright's disease. The authors conclude that the correlation of function and anatomical structure which is the basic and all important part of the problem is still a complete mystery. "It is by experimentation under control and simplified conditions that this ultimate phase must be attacked. And it is from such endeavor that a more satisfactory theory and classification of Bright's disease will eventually evolve." M. H. BARKER.

AN authoritative work[5] incorporating the many advances in our knowledge of nutrition is indispensable to the student and to the practitioner.

[1] OBSTRUCTIVE JAUNDICE: PHYSIOLOGIC AND SURGICAL ASPECTS. By Waltman Walters, M.D., F.A.C.S., M.S.(Minn.). Published from The Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota. Owatonna: Journal-Chronicle, 1931.

[2] L'OSTEOSYNTHÈSES DES OS LONGS: ÉTUDE CRITIQUE, BIOLOGIQUE ET PRATIQUE. By C. E. Cornioley. Preface by Prof. Ch. Julliard. Paris: G. Doin et Cie., 1931.

[3] OPERATIVE CHIRURGIE DER KNOCHENBRUCHE. vol i. OPERATIONEN AM FRISCHEN UND VERSCHLEPPLEN KNOCHENBRUCH. By Professor Fritz Koenig. Berlin: Julius Springer, 1931.

[4] THE RENAL LESION IN BRIGHT'S DISEASE. By Thomas Addis and Jean Oliver. New York: Paul B. Hoeber, Inc., 1931.

[5] NUTRITION AND DIET IN HEALTH AND DISEASE. By James S. McLester, M.D. 2d ed. rev. Philadelphia and London: W. B. Saunders Company, 1931.

Four reprintings since the initial appearance of McLester's book in 1927, and the present revised edition are tributes to its worth; it remains one of the best available on the subject. Recent discoveries particularly in regard to vitamines, minerals, and deficiency diseases are included; sections dealing with the toxæmias of pregnancy, food poisoning, irritable colon and protozoan infections have been added. The first part contains a full and lucid discussion of the physiology of nutrition and of diet in health. In the second part, devoted to nutrition in disease, underlying pathologic conditions are described in order to make clear the rationale of suggested measures of treatment. A third section contains tables and charts of a general nature. An excellent bibliography at the end of each chapter adds to the value of a book which should prove useful to all practitioners. WALTER H. NADLER.

THE three volumes at hand of the biographical dictionary[1] of outstanding physicians of all times and countries represent an augmentation and reprinting of Gurlt's biographical dictionary which was published in the eighth decade of the last century and is now out of print. It has been the aim of the present editors, Huebotter and Vierordt, to add the biographies of outstanding medical men who have attained prominence since the last edition was printed and to amend the material of the first edition where new facts and discoveries have made these corrections necessary. In this they have succeeded.

The list of the contributors of the biographies is a noteworthy one and bears silent testimony to the authoritativeness of the work. The first volume comprises 898 pages of biographies, 16 plates depicting portraits of 64 famous physicians, and 28 pages of references from which the material was obtained. The second volume contains 926 pages of biographies and 16 plates depicting 64 portraits. The third volume contains 873 pages of biographies and the same number of plates and portraits as the preceding volume. The 3 volumes carry the biographies through that of Daniel L. Lyons, an English physician of Bath, who was particularly interested in the use of calomel in fevers and dropsy.

This monumental work will be of great value to the student of medical history and the succeeding volumes will be awaited with pleasant anticipation.

ALFRED BROWN.

THE third of the series of monographs edited by Prof. Ludwig Archoff and others under the general title of "Pathologie und Klinik in Einzeldarstellungen"[2] is entitled "Die Lebensvorgaenge im normalen Knorpel und seine Wucherung bei Akromegalie," and was written by J. Erdheim, professor of pathology in the University of Vienna. The book compares favorably with the very high standards set by the preceding studies of the series. Professor Erdheim has presented a very detailed description of the changes which occur in costal and articular cartilage in acromegaly and has divided his discussion into four parts. This volume is illustrated with thirty-one photomicrographs and is well indexed. It is a highly scientific contribution to a very narrow field of medicine but it will be a useful aid to those who are interested in the anatomy and pathology of bone and cartilage. J. P. SIMONDS.

THE author of *Abdominal Pain*[3] very briefly reviews the various theories of the evolution of abdominal pain by Ross, Lennander, Mackenzie, Head, Hurst, and Kappis. Morley believes as Hurst does that visceral pain is usually the result of abnormal tension on the splanchnic afferent nerve endings in the muscular walls of the hollow viscera. This pain is deep seated and not accurately localized. The author believes that somatic pain is not visceral pain and is in no way concerned with the afferent autonomic system. This pain is referred from the highly sensitive cerebrospinal nerves of the parietal peritoneum. For this latter he uses the terms peritoneocutaneous radiation and peritoneomuscular reflex.

Part of the book is taken up with brief discussions of the possible mechanisms in the production of pain in many abdominal conditions. These include visceral disease, such as disorders of stomach, duodenum, biliary system, pancreas and spleen, acute appendicitis, intestinal pain, and the urogenital system. Referred pain is discussed in detail and a good differentiation between pain of splanchnic and cerebrospinal origin is given.

The book is easy to read and understand. The discussions are excessively brief. Many conflicting points with his theory are taken lightly and not explained thoroughly. Morley has written a good brief résumé on abdominal pain. THEODORE T. STONE.

AN extremely valuable and interesting book is presented by Dr. Kessler in his book on accidental injuries.[4] His opinions are based not only on his personal examination of 63,000 cases at the New Jersey Compensation Bureau but also upon a rich acquaintance with the American and foreign literature on this subject. It is a valuable guide in the study of the proper evaluation of injuries, the prognosis and probable period of disability, and is very helpful in estimating the functional capacity of injured members. Large sections are devoted to the relationship of injury and disease and to the rehabili-

[1] BIOGRAPHISCHES LEXICON; DER HERVORRAGENDEN AERTZTE ALLER ZEITEN UND VOELKER. By various collaborators, edited by Dr. E. Gurlt, Dr. A. Wernich, and Dr. August Hirsch. 2d ed. rev. and enlarged by Prof. F. Huebotter and Prof. H. Vierordt. Vols. i, ii, and iii. Berlin and Vienna: Urban & Schwarzenberg, 1929.

[2] PATHOLOGIE UND KLINIK IN EINZELDARSTELLUNGEN. VOL. III.—DIE LEBENSVORGAENGE IM NORMALEN KNORPEL UND SEINE WUCHERUNG BEI AKROMEGALIE. By Professor Dr. J. Erdheim. Berlin and Vienna: Julius Springer, 1931.

[3] ABDOMINAL PAIN. By John Morley, Ch.M., F.R.C.S. With an Introduction by J. S. B. Stopford, M.D., F.R.S. New York: William Wood & Co., 1931.

[4] ACCIDENTAL INJURIES; THE MEDICO-LEGAL ASPECTS OF WORKMEN'S COMPENSATION AND PUBLIC LIABILITY. By Henry H. Kessler, A.B., M.D., F.A.C.S., F.A.P.H.A. Foreword by Fred H. Albee. Philadelphia: Lea and Febiger, 1931.

tation of the injured. The injuries of the various regions of the body are considered separately. The sections on fractures and hernia are particularly interesting. The reviewer feels that this excellent book should be in the hands of all men dealing with industrial injuries. FREDERICK CHRISTOPHER.

IN the introduction to his book on roentgen technique, Block states that his work[1] is not for the trained roentgenologist but rather for the technician and physician doing occasional X-ray work. The book takes up elementary problems in physics, such as milliamperes, ohms, and volts, electromagnetism, induction, transformers, etc. He gives a thorough discussion of the physics of rays, X-ray tubes, and measuring instruments. He includes a complete chapter on the various types of X-ray equipment used in Germany, with comparative tables of maximum output and load of these types of machines, but this is of little value to anyone in this country. The book contains a discussion of electrical accidents and a paragraph on resuscitation. The book is well written, although there is very little in it that is new, and is practically limited to home consumption.

ROBERT A. ARENS.

FOR the aid of the man doing roentgen therapy with limited equipment, particularly the 10 inch apparatus, Erskine has written an interesting book.[2] He does all his treatments with three techniques, thereby simplifying the work considerably, but adds a fourth technique for those who have 200 kilovolt equipment. The chapters on physics are clear and concise, and it is refreshing to see the absence of complicated formulæ. All his work is measured by the universal R unit. He describes various measuring instruments and gives their good qualities as well as calls attention to their shortcomings. The book contains 24 excellent illustrations including curves and tables. The conditions suitable for X-ray treatment are divided into three sections: skin, non-malignant, and malignant conditions. The author does not claim to include all possible diseases that can be treated by X-ray. ROBERT A. ARENS.

[1] EINFUEHRUNG IN DIE MEDIZINISCHE ROENTGENTECHNIK. By Maximilian F. Block. Vienna: Wilhelm Maudrich, 1931.

[2] PRACTICAL X-RAY TREATMENT. By Arthur W. Erskine, M.D. St. Paul and Minneapolis: The Bruce Publishing Company, 1931.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be granted as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

INTRODUCTION TO DIATHERMY FROM THE MEDICAL AND TECHNICAL POINT OF VIEW. By H. Henseler, M.D., and E. Fritsch, Dipl. Eng. Berlin: Radionta-Verlag, 1929.

DER GEBURTSCHILFLICHE PHANTOMKURS. By Dr. Wilhelm Liepmann. 2d. rev. ed. Berlin and Vienna: Urban & Schwarzenberg, 1931.

DYNAMIC RETINOSCOPY. By Margaret Dobson. London: Oxford University Press, 1931.

AIDS TO SURGICAL ANATOMY. By Richard H. Hunter, M.D., M.Ch., Ph.D. New York: William Wood and Company, 1931.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.). 3d rev. ed. New York: William Wood and Company, 1931.

A MANUAL OF CLINICAL LABORATORY METHODS. By Clyde Lottridge Cummer, Ph.B., M.D., F.A.C.P. 3d rev. ed. Philadelphia: Lea & Febiger, 1931.

GUIDE TO LOCALIZED BI-TERMINAL TONSILLAR COAGULATION. By L. Leo Doane, A.M., M.D., Ph.D., F.A.C.S. Butler, Pa.: Washburn & Co., 1931.

A TEXT-BOOK OF NEURO-ANATOMY. By Albert Kuntz, Ph.D., M.D. Philadelphia: Lea & Febiger, 1931.

EINFUEHRUNG IN DIE DIATHERMIE VOM MEDIZINISCHEN UND TECHNISCHEN STANDPUNKT. By Dr. med. H. Henseler and Dipl. Eng. E. Fritsch. 3d ed. Berlin: Radionta-Verlag, 1931.

GONORRHEA IN THE MALE AND FEMALE; A BOOK FOR PRACTITIONERS. By P. S. Pelouze, M.D. 2d rev. ed. Philadelphia and London: W. B. Saunders Company, 1931.

APPROVED LABORATORY TECHNIC; CLINICAL, PATHOLOGICAL, BACTERIOLOGICAL, SEROLOGICAL, BIOCHEMICAL, HISTOLOGICAL. Prepared under the auspices of The American Society of Clinical Pathologists. By John A. Kolmer, M.D., Dr.P.H., D.Sc., LL.D., and Fred. Boerner, V.M.D. New York and London: D. Appleton and Company, 1931.

HERTZLER'S MONOGRAPHS ON SURGICAL PATHOLOGY. Surgical Pathology of the Genito-Urinary Organs. By Arthur E. Hertzler, M.D., Philadelphia, Montreal, and London: J. B. Lippincott Company, 1931.

BRAIN TUMORS; THEIR PATHOLOGY, SYMPTOMATOLOGY, DIAGNOSIS AND PROGNOSIS. By Leo M. Davidoff, M.D. Reprinted from Psychiatric Quarterly, vols. iv and v, April, 1930, to April, 1931. Utica, N. Y.: State Hospitals Press, 1931.

CLINICA QUIRURGICA. By Pablo L. Mirizzi. Vol. ii. Córdoba, Argentina: El Ateneo, 1931.

HERTZLER'S MONOGRAPHS ON SURGICAL PATHOLOGY. Surgical Pathology of the Diseases of Bones. By Arthur E. Hertzler, M.D. Philadelphia, Montreal, and London: J. B. Lippincott Company, 1931.